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Editorial Issue (0)

We are pleased to present to you issue 0 of the academic *Journals of Medical and Pharmaceutical Sciences* for the year 2021. We thank you very much for the great efforts made by ***Prof. Dr. Ziad M. Abood***, showing the current issue of the magazine. We also extend our thanks to the editor-in-chief, ***Prof. Dr. Taghreed Khudhur Mohammed*** in the follow-up of prestigious research and printing, issue 0. The current issue of the journal included a number of research and scientific articles related to: the effect of pomegranate peel extracts against bacteria, the COVID-19 epidemic, the prevalence and risk factors of obesity in children, the effect of the ACE2 RS2106809 and RS2074192 genotype on the tolerance of both sexes to infection and recovery from Covid disease-19, Anti-Zinc Oxide Nanoparticles and Antioxidants, Food and Nutrition Safety during the COVID-19 Pandemic Period, Pharmaceutical Monitoring, and Sense of Smell and Taste in People with COVID-19 Infection. We hope that the Academy for Medical and Pharmaceutical Sciences will achieve, through this edition, the aspirations of researchers and those interested, and that we seek, with the help of God Almighty, to develop the scientific journal for the better, and to have a distinguished scientific presence regionally and globally, and we look forward to elevating the journal to the international scientific classifications accredited internationally and for the purposes of scientific promotion.

With sincere appreciation

Asst. Prof. Dr. Saad Badi Nshter
Editor-in-Chief, February - 2021

About Iraqi Academics Association

The Iraqi Academics Association was established pursuant to Law No. 61 of (2017), with the aim of caring for the teaching and academic staff and upgrading the level of workers in this vital sector and preparing plans and policies that improve the teaching process and for the establishment of councils and unions concerned with the affairs of academics and their defense and preservation of their dignity and academic freedoms. And in order to raise the reputation of Iraqi universities and institutes and equalize them with their counterparts in civilized countries. According to clause -3 of the second clause of its law, it:

First: The Iraqi Academics Association has the moral personality and financial and administrative independence represented by (the Iraqi Academics Association) or whoever is authorized by it.

Second: The union's center shall be in Baghdad, and it may open branches in the governorates and wherever the union's interest requires finding representation for it.

Third: Members of the College in Iraqi universities and institutes recognized by the Ministry of Higher Education and Scientific Research may belong to the Association.

According to Article -3-, the objectives of establishing the union are:

First: Upgrading the profession of higher education and scientific research to achieve its mission of serving the nation and the nation's generations.

Second: Coordination and cooperation with the Ministry of Higher Education and Scientific Research and the relevant authorities in order to achieve the union's tasks.

Third: Promoting the ethics of the higher education profession and preserving the ethics, traditions and honor of the profession.

Fourth: Encouraging studies, research, educational activities and conferences, and holding courses and seminars to raise the scientific and professional level of teachers in Iraqi universities and institutes.

Fifth: Strengthening the position of academics in society and defending their rights, interests and dignity.

Sixth: The advancement and advancement of members professionally, economically, culturally and socially.

Seventh: Establishing a Social Solidarity Fund to help union members, ensuring them and their families a decent life in cases of complete disability or death, and providing health care for members and their families.

Eighth: Cooperation and strengthening of relations with similar Arab and international federations.

Asst. Prof. Dr. Muhannad Al-Hilal
Head of the Iraqi Academics Association

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Publishing Rules

• The magazine publishes scientific studies with original, modern and renewed ideas. It contains letters and theses that have not been previously published or contributed to in one of the scientific forums, and that these researches are included in one of the axes, engineering and pure science majors.

• The magazine also publishes authored and translated books within the above disciplines.

• The papers submitted to the journal must be free of linguistic, methodological and cognitive errors, and adhere to the scientific norms followed, and have not been previously published.

• The number of search pages should not exceed fifteen sheets of B5 size.

• In the event that there are margins at the bottom of the page, an automatic numbering should be adopted that is renewed on every page.

• The research includes two abstracts: the first in the language of the research, and the second in the Arabic or English language.

• All research is subject to secret scientific arbitration, and the researcher is informed either to accept his research, or to conditional acceptance of some modifications that he is informed of, or to refuse. And in this last case; The journal is not obligated to explain the reasons.

Technical Recommendations in Research Writing:

• Paper size and margins: The paper is B5 size, leaving a margin of 2 cm from the margins of the paper. With a 1 cm spacing between lines in the body and the margins.

• ***Simplified Arabic*** (Article in Arabic)/ and ***Times New Roman*** (Article in English), size 16 bold for the title of the research, size 14 bold for the main headings, size 12 bold for subheadings, and size 12 in the body, size 11 bold for titles of figures and tables. 10 in the footnotes.

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رقم الإيداع في دار الكتب والوثائق ببغداد 778 لسنة 2021

Study the Effect of Pomegranate Peel Extracts Against Bacteria Isolated from Different Sources

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Abstract

Escherichia coli and *Staphylococcus aureus* were isolated from hash meat and burger meat respectively, the pomegranate peel extracts were extracted by alcoholic (ethanol 96%) and sterile distilled water in order to study the antibacterial effects of these extracts against the isolated bacteria. The aim of this study was to compare between the effect of these extracts against food and clinical isolates. Agar well diffusion method was used in order to study the antibacterial effects of alcoholic and aqueous extracts of pomegranate peel against all the tested bacteria. The results of this study showed that alcoholic extracts of pomegranate peel extracts have antibacterial activity against all the tested bacteria (food and clinical) isolates of *E.coli* and *S.aureus*, while the aqueous extracts showed antibacterial activity against all the tested bacteria except the food isolates of *E.coli*. The diameter of inhibition zone ranged from 12.5 - 33mm.The highest inhibition zone(33)was from aqueous extracts against food isolate of *S.aureus*, and the lowest inhibition zone (15mm) from the same extract against clinical isolate of *E.coli*. The highest inhibition zone of alcoholic extracts of pomegranate peel extracts was (27.5mm) against food isolate of *S.aureus* and the lowest inhibition zone for the same extract was (12.5mm) against clinical isolate of *S.aureus*. The control D.W and ethanol that used in this study have no antibacterial activity against all the tested bacteria. From the above results we can conclude that our local food samples contaminated with pathogenic bacteria *E.coli* and *S.aureus* and we can control to the contamination by adding pomegranate peel extracts either

aqueous or alcoholic in order to preserve these product from spoilage also to act as natural antibacterial compound that prevent its transmission to consumer, also these extracts can used to control the pathogenic bacteria from clinical sources.

Keywords: Pomegranate peel extracts, antibacterial activity, agar well diffusion method, bacteria isolated from food, clinical bacterial isolates.

Introduction

The microbial activity is a major mode of deterioration of several foods and is often responsible for the loss of quality and safety. The concern pathogenic and spoilage microorganisms in foods are increasing due to the increase in outbreaks of food borne disease [1]. Recently there is a growing interest to use natural antimicrobial compounds, like plant extracts of herbs and spices for the preservation of foods, as these possess a characteristic flavour and sometimes show antioxidant activity as well as antimicrobial activity. Several food-preservation techniques have traditionally been utilized to control microorganisms in food. These preservation techniques include chilling, freezing, drying, salting, smoking, fermentation, and non-thermal physical treatments or the addition of synthetic antimicrobials and antioxidants [2]. Increasing concerns over negative impacts on health issues associated with the use of synthetic preservatives were detected [3]. Therefore, the importance of replacing synthetic antioxidants with natural ingredients from spices and other plant materials has greatly increased. The pomegranate (Punica granatum) belonging to the family punicaceae is one of the important dietary sources of antioxidant phenolic [4]. Pomegranate peel is recognized for its many health-promoting qualities and apparent wound healing properties [5], antimicrobial activity [6], anticancer property [7], antiatherosclerotic and antioxidative capacities [8]. This antioxidant capacity has been mainly attributed to the water-soluble polyphenols,

anthocyanins and hydrolysable tannins. Research indicates that pomegranates and their extracts may serve as natural alternatives due to their potency against a wide range of bacterial and viral pathogens. Nearly every part of the pomegranate plant has been tested for antimicrobial activities, including the fruit juice, peel, arils, flowers, and bark. Many studies have utilized pomegranate peel with success. There are various phytochemical compounds in pomegranate that have demonstrated antimicrobial activity, but most of the studies have found that ellagic acid and larger hydrolyzable tannins, such as punicalagin, have the highest activities. In some cases the combination of the pomegranate constituents offers the most benefit. The positive clinical results on pomegranate and suppression of oral bacteria are intriguing and worthy of further study. Much of the evidence for pomegranates 'antibacterial and antiviral activities against foodborne pathogens and other infectious disease organisms comes from in vitro cell based assays. The aim of present investigation was to assess the antibacterial activity of pomegranate peel extracts against food isolated bacteria in comparison with clinical pathogenic isolates.

Materials and Methods

Preparation of pomegranate peel extracts

The pomegranate peels were collected. The pulp was separated manually from the peel and washed to remove the unwanted materials. The washed peels were cut into small pieces and dried in hot air oven at 60°C for 12h. The dried peels were ground in the kitchen grinder to make the fine powder to pass through 1 mm sieve. The extraction was carried out according to the methods described by [9] with slight modification. About 25g of peel powder was mixed with 150 ml of ethanol 96%. The mixture of peel powder and ethanol subjected to shaking at ambient temperature for 12 h at the speed of 190 rpm. The mixture was filtered and residue was re extracted with same solvent. The filtrates of the mixture were placed under a hood in the rotavapor to remove the residual ethanol under vacuum. The extracts were stored

at -20°C in a sample container for further analysis. The procedure likewise performs with sterile distilled water instead of ethanol inorder to obtain aqueous pomegranate peel extract. For stock solution each extract (alcoholic and aqueous) was redissolved with 5ml sterile D.W.

Culture media used in this search

The following culture media used in recent study:

1-MacConkey Agar.

2-Mannitol Salt Agar.

3-Mueller Hinton Agar.

4-Brain-Heart infusion broth.

A-Isolation and identification of food isolated bacteria

Minced (hash meat and burger) samples were used in order to isolate *E.coli* and *S.aureus*. 5gm from each food sample +45ml DW. 0.1ml from dilution 10^{-1} cultivated on MacConkey agar and Mannitol salt agar by pouring plate method, Incubate dishes in incubator at 37°C for 18-24 hour. Biochemical tests were used for identification of the obtained isolates, Gram stain technique also used for identification. For confirmation of the diagnosed isolates VITEK 2 system was used.

Note: Two isolates *E.coli* and *S.aureus* were obtained from Biology department, pathogenic bacteria laboratory, College of Science in order to compare the results of antibacterial activity of pomegranate peel extracts, in further study.

B-Antibacterial activity of pomegranate peel (alcoholic and aqueous) extracts against food and clinical isolates of *E.coli* and *S.aureus*

Agar well diffusion method was used as follows:

1- Activation of food and clinical isolates separately in BHI broth and incubate the tube at 37 °C for 18-24hr.

2- Dilute the bacterial broth in normal saline by comparison with McFarland 0.5 tube ($1x10^8$ CFU/ml).

3- Mueller Hinton agar plates prepared in sterile condition.

4- Inoculate MHA plates with the diluted tested bacteria by Swabbing method.
5- Four wells were made with sterial corkborer in each plate under sterile condition.
6- 200µl from alcoholic and aqueous pomegranate peel extracts were put in two wells and other two wells filled with ethanol 96% and sterile distilled water as controls.
7- Incubate the plates at 37°C for (18-24 hr).
8- Measure inhibition zone in mm by ruler.
9- Each test done in duplicate.

Results and discussion

A- Isolation and Identification of Bacteria from Food Samples

E.coli appear as pink colonies on MacConkey agar due to production of acid from lactose, absorption of neutral red and a subsequent colour change of the dye when the pH of medium decreases below 6.8,as shown in figure (1). The bacteria under the microscope appear in the form of short rod or bacilli pink cells, which is negative for gram stain after examination under microscope. Biochemical tests were used inorder to identification of the isolated bacteria.

Colonies of *S.aureus* bacteria appeared as yellow color on Mannitol salt agar because it ferments Mannitol, an acidic byproduct is formed that causes the phenol red in the agar to turn yellow, as shown in figure (2). Biochemical tests were used to identify the isolates. Also Gram stain was used for morphological identification under light microscope. *S.aureus* appear cocci forms in purple clusters since it is Gram positive bacteria.

Figure (1) pink colonies of *E.coli* on MacConkey agar

Figure (2) Yellow colonies of S.aureus on Mannitol salt agar

To confirm the identification of the isolates VITEK 2 system was used.

B-Antibacterial activity of pomegranate peel extracts (alcoholic and aqueous) against food and clinical isolates of *E.coli* and *S.aureus*

The results showed that both alcoholic and aqueous extracts of pomegranate's peel illustrated antibacterial activity against all the tested bacteria except against *E.coli* from food source as shown in table (1).The largest inhibition zone was from aqueous extracts of

pomegranate peel against *S.aureus* from food origin (33mm), while the lowest inhibition zone was (12.5mm) from alcoholic extracts of pomegranate peel against *S.aureus* from clinical origin.

Table (1) Antibacterial activity of pomegranate peel extracts (in mm) inhibition zone against food and clinical isolates of *E.coli* and *S.aureus*

Bacteria	Aqueous extract	Ethanolic 96%extract	D.W control	Ethanol 96% control
Food *E.coli*	--------	17.5	----------	----------
Food *S.aureus*	33	27.5	----------	----------
Clinical *E.coli*	15	17	---------	----------
Clinical *S. aureus*	13.5	12.5	---------	---------

The antimicrobial agents have long been researched for their effectiveness to inhibit growth of microorganisms in the foods. This has been done in an effort to increase food safety for the consumer, as well as to increase the shelf life of food products [10]. From the present study, the results showed that pomegranate peel extracts either aqueous or alcoholic can inhibit the growth of bacteria regardless its origin (food or clinical). These results were in agreement with previous studies for many researchers. Our results are also in support with the findings of [11] who found that methanol extract of pomegranate fruit was active against *E. coli, S. aureus,* and *B. subtilis* with the diameter of inhibition zone of 12, 22, and 12 mm, respectively. According to[12] the pomegranate peel extract showed good antimicrobial activity against *Staphylococcus aureus, Pseudomonas* and *E. coli*. The difference in inhibition zone of peel extracts against tested food borne pathogens may be due to the different extraction methods followed, freshness of fruits peel used and the variations in the season and region

of growth [13]. The higher antimicrobial activity against gram positive bacteria was because the gram-positive bacteria has less stable cell wall which allow the permeation of some antimicrobial agents. The lowest antimicrobial activity against gram negative bacteria was due to the presence of outer cell membrane of bacterium composed of phospholipids bilayer and proteins, avoids the permeation of antimicrobial agents inside the cell wall. Pomegranate showed good antimicrobial activity against *Staphylococcus* aureus and Bacillus cereus having minimum inhibitory concentration of 0.01%. *Pseudomonas* could be inhibited at a higher concentration of 0.1% while it was ineffective against Escherichia coli and *S. typhimurium* [14]. In Thailand, a study was undertaken in which extracts of pomegranate were tested for their antibacterial activity against different strains of *E. coli*, including 3 strains of *E. coli* O157:H7 [15]. Growth inhibition zones, using the agar disc diffusion method, ranged from 7 to 17 mm. An aqueous extract of pomegranate was highly effective against *E. coli* O157:H7 with minimum inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) values of 0.19 and 0.39mg/ml, respectively. In another Thai study, an ethanolic extract of pomegranate had MICs of 0.49 to 1.95mg/ml and MBCs of 1.95 to 3.91mg/ml against *E. coli* O157:H7 [16]. This extract exhibited both bacteriostatic and bactericidal activities, indicating that it may be an effective adjunct treatment for *E. coli* O157:H7 infection. In Najaf city [17] showed that 100mg/ml of alcoholic pomegranate fruit peel extract had a good antibacterial activity against hair isolates of *S.aureus*.

Conclusion

Natural antimicrobials compounds can extend the shelf life of food products, and due to absence of synthetic agents, these compounds are safe without any side effects on human health. The results of present investigation revealed that the extracts of pomegranate act as a good

source of natural antimicrobials compounds and it could use as a antimicrobials agents in the food and food products to inhibit spoilage or pathogenic microorganism that could be transmitted via food, also this natural extracts could be used as antibacterial agent for bacteria isolated from clinical samples.

References

1. Tauxe RV. 1997. Emerging foodborne diseases: an evolving public health challenge. Dairy, Food Environmental Sanitation. 17:788-795.

2. Davidson PM, Naidu AS. 2000. Phyto-phenols. In: Naidu AS, editor. Natural Food Antimicrobial Systems. Boca Raton: CRC Press. 265-294.

3. Sofos JN, Geornaras I. 2010. Overview of current meat hygiene and safety risks and summary of recent studies on biofilms, and control of *Escherichia coli* O157:H7 in nonintact, and *Listeria monocytogenes* in ready-to-eat, meat products. Meat Sci. 86(1):532-539.

4. Ozgen, M., C. Durgac, S. Serce and C. Kaya, 2008. Chemical and antioxidant properties of pomegranate cultivars grown in Mediterranean region of Turkey. Food Chem., 111: 703-706.

5. Chidambara, M. K., V. K. Reddy, J. M. Veigas and U.D. Murthy, 2004. Study on wound healing activity of Punica granatum peel. J. Med. Food, 7: 256-259.

6. Braga, L.C., A. A. Leite and K.G. Xavier, 2005. Synergic interaction between pomegranate extract and antibiotics against *Staphylococcus aureus*. Can. J. Microbiol., 51: 541-547.

7. Jeune, M.A., J. Kumi-Diaka and J. Brown, 2005. Anticancer activities of pomegranate extracts and genistein in human breast cancer cells. J. Med. Food, 8: 469-475.

8. Tzulker, R., I. Glazer, I. Bar-Ilan, D. Holland, M. Aviram and R. Amir, 2007. Antioxidant activity, polyphenol content and related compounds in different fruit juices and homogenates prepared from 29

different pomegranate accessions. J. Agric. Food Chem., 55: 9559-9570.

9. Iqbal S, Haleem S, Akhtar M, Zia-ul-haq M, Akbar J. 2008. Efficiency of pomegranate peel extracts in stabilization of sunflower oil under accelerated conditions. Food Res. Int. 41:194-200.

10. Khan JA, Hanee S. 2011. Antibacterial properties of punica granatum peels. Int. J App. Biol. Pharma. Tech. 2(3): pp. 23-27.

11.Melendez PA, Capriles VA. 2006. Antibacterial properties of tropical plants from Puerto Rico. Phytomedicine. 13:272-279.

12. Kanatt SR, Chander R, Sharma A. 2008. Chitosan and mint mixture: A new preservative for meat and meat products. Food Chem. 107:845-852.

13. Mccarrell E, Gould S, Fielder M, Kelly A, El-sankary W, Naughton D. 2008. Antimicrobial activities of pomegranate rind extracts: enhancement by addition of metal salts and vitamin C. BMC Complem. Altern. Med. 8:64-70.

14. Kanatt, S. R.; Chander, R. and Sharma,A. 2010.Antioxidant & antimicrobial activity of pomegranate peel extract improves the shelf life of chicken products. Int. J-food sc.& Technol.45.216-222.

15. S. Voravuthikunchai, A. Lortheeranuwat, W. Jeeju, T. Sririrak, S. Phongpaichit, and T. Supawita. 2004.Effective medicinal plants against enterohaemorrhagic *Escherichia coli* O157:H7,‖ Journal of Ethnopharmacology, vol. 94, no. 1, pp. 49–54.

16. S. P. Voravuthikunchai and S. Limsuwan. 2006. Medicinal plant extracts as anti *Escherichia coli* O157:H7 agents and their effects on bacterial cell aggregation, ‖ Journal of Food Protection, vol. 69, no. 10, pp. 2336–2341.

17. M. Abdulbary. 2017. The antimicrobial activity of alcoholic and aqueous extracts of pomegranate fruit peel on *Staphylococcus aureus* isolated from hair in Najaf. Kufa Journal for Veterinary Medical Sciences, Vol. (8) No. (2). pp .238-244.

A General Overview on the epidemiology of COVID-19 Pandemic

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Abstract

Coronaviruses are enveloped viruses with nonsegmented, single-stranded RNA, and positive-sense genomes. *Coronaviridae* cause a wide-ranging spectrum of human and animal diseases. At the end of September 2019, a new coronavirus outbreak called Covid 19 which was caused by SARS-CoV-2 in Wuhan, China. Severe acute respiratory syndrome (SARS) that occurred. In March 2020, the WHO announced that COVID-19 is a global pandemic. Coronaviruses can be transmitted in the following ways: sneezing and coughing of an infected person without covering the mouth can disperse droplets into the air. Shaking hands or touching with a person, who has the virus, may pass the virus among people. Also, the direct contact with a surface that has the virus and then touching the nose, mouth or eyes. Coronaviruses incubation period is 4-14 days after exposure to pathogen. Individuals of all ages may acquire SARS-CoV19 infection, although older individuals and middle age are the majority. The clinical symptoms involve fever, dry cough, fatigue, rhinorrhea, sore throat, conjunctivitis headache, dyspnea, myalgia, nausea, vomiting and diarrhea. COVID-19 disease may develop to pneumonia, pulmonary failure then death. The aim of this review is to discuss the epidemiology of Covid 19 disease in term of its pathogenicity, and to shed the light on the ways of its diagnosis, prevention and treatment.

Keywords: Coronavirus, Pandemic, Covid-19, SARS, RNA, Wuhan.

Introduction

Coronavirus is single stranded, enveloped RNA viruses and covered with glycoprotein [1, 2]. Coronaviruses belong to the order *Nidovirales* and the family Coronaviridae. Coronaviruses are classified into four genera which are: α-, β-, γ-, and δ- CoV. The genera α- and β- CoVs only infect mammals, but γ- and δ- CoVs infect birds. Human CoVs consists of α- CoVs, β- CoVs, the Middle East respiratory syndrome (MERS-CoV), and SARS-CoV [3]. At the end of December 2019, a novel coronavirus was identified as the reason of pneumonia cases of unidentified etiology (COVID-19) in Wuhan, China [4]. In February 2020, the WHO recognized the disease as COVID-19. The virus that causes COVID-19 is known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [5]. COVID-19 is the third strain of coronavirus to emerge in human populations in the past two decades after of the outbreak severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and outbreak of the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012. China has informed the World Health Organization about the outbreak. The World Health Organization (WHO) has responded quickly by developing diagnostic methods, issuing instructions on patient monitoring, specimen collection, and treatment as well as regularly updating information about the outbreak [6]. These viruses are responsible for a number of outbreaks around the world, including the severe acute respiratory syndrome (SARS) in 2002-2003, the Middle East respiratory syndrome (MERS) in 2015 in South Korea and most recently, the COVID-19 outbreak at the end of 2019 in China [5]. While some coronaviruses have caused epidemics, others cause mild to moderate respiratory infections, like the common cold [7]. The aim of the current review is to shed the light on COVID-19 disease in term of its epidemiology, clinical symptoms, transmission and diagnosis, as well as the currently available treatment options for that disease.

Epidemiology

The first case of COVID-19 disease was discovered in December 12, 2019 with unknown pneumonia. On January 22, 2020, a novel CoV was declared to be originated from wild bats and belonged to beta-coronavirus Group 2 that contains severe acute respiratory syndrome associated coronavirus SARS-CoV [8]. Although SARS-CoV and SARS-CoV-2 belong to the subgroup beta coronavirus, the similarity in their genomes is only 70%, and the SARS-CoV-2 was found to show genetic differences from SARS-CoV. Similar to the SARS disease, the COVID-19 disease outbreak occurred in China during the spring festival, which was between January 10 and February 18. The spring festival activities created good conditions for transmission of the disease and severe difficulties in control and prevention of the epidemic [9]. There was a rapid increase in COVID-19 cases epidemic between January 10-22 [10]. Wuhan, the center of the epidemic, is also an important transportation network center in the spring festival that created good conditions for spread of this epidemic [11].

Transmission

Coronaviruses can be transmitted in the following ways: sneezing and coughing without covering the mouth can disperse droplets into the air. Shaking hands or touching with a person who has the virus may pass the virus among people. Contact with a surface that has the virus and then touching the nose, mouth or eyes [12]. According to a study [6] published in 2019, an-giotensin converting enzyme 2 (ACE.2) a membrane exopeptidase in the receptor used by corona virus to entry into human cells. To prevent spread of COVID- 19, people should stay at home, avoid direct contact with others, and cover the nose and mouth with a handkerchief while sneezing or coughing [3].

Symptoms

Symptoms vary from person-to-person, cold- or flu-like symptoms usually appear from 2–4-14 days after a coronavirus infection and are typically mild [14]. The usual clinical symptoms involve fever, dry cough, fatigue, sneezing, runny nose, sore throat, rhinorrhea, headache, myalgia, nausea and vomiting while diarrhea and dyspnea are uncommon feature [15].

Diagnosis

Real time polymerase chain reaction (RT-PCR) has become the method of choice for diagnosis of COVID-19. As multiplex real-time RT-PCR assays have been developed, are able to detect all four respiratory HCoVs. Serologic assays detect anti-viral (IgM) and (IgG) antibodies. Serologic assays are important in cases where RNA may be difficult to isolate [16, 17].

Laboratory Diagnosis (RT-PCR vs. Serology)

COVID-19 is identified by RT-PCR. Samples from sputum, throat swabs (nasopharyngeal in children), lower airway secretions, blood and stool could be checked for COVID -19 ribonucleic acids [18]. An oropharyngeal swab can be gathered, but is not crucial; if gathered, it should be put in the same container as the nasopharyngeal swab specimen. Negative RT-PCR results from oropharyngeal swabs, regardless of CT findings indicative of viral pneumonia, have been demonstrated in certain cases that ultimately shown to be positive for SARS-CoV-2 [19]. Sputum should only be obtained from cases with productive cough; however, sputum induction is not advised. If preliminary testing is negative, but the doubt for COVID-19 persists, the WHO advises recollection and analyzing from several airway sites. Laboratory testing of the SARS ribonucleic acid may result in false-negative results, and serological analysis of virus-specific IgG and IgM antibodies should be utilized as an option for diagnosis [20]. Typical

disease manifestations and radiological lung abnormalities in a case with negative four times RT-PCR tests for SARS-CoV-2 and positive IgG and IgM antibodies against the virus were demonstrated [17]. It has been earlier shown that some SARS-CoV-2 infected cases are asymptomatic while RT-PCR tests are verified positive, and some cases that improved from COVID-19 disease may still have positive RT-PCR results during follow-up. Additional laboratory tests, including complete blood count and biochemistry, are generally nonspecific. The leukocyte count is frequently normal or low. There might be lymphopenia; a lymphocyte count <1,000 has been related to severe disease. The thrombocyte count is generally normal or slightly low. Most cases show high CRP and ESR, but procalcitonin levels are typically normal. An elevated procalcitonin level may point to a bacterial co-infection. The ALT/ AST, prothrombin time, creatinine, D-dimer, CPK, LDH, myohemoglobin and ferritin levels might be increased and elevated levels might be related to severe disease [16, 21, 22]. On hospitalization, many cases with pneumonia have normal serum procalcitonin levels, but, in cases necessitating intensive care unit (ICU) management, they are more likely to be increased. Elevated D-dimer levels and more severe lymphopenia have been shown to be linked with fatality [23]. The lung X-ray (CXR) generally shows bilateral infiltrations but may be normal in the early phase of the disease. The chest CT is more sensitive and specific. Lung CT scans generally demonstrate infiltrates, ground-glass opacities and subsegmental consolidation. Less common abnormalities contain pleural effusion/thickening, and lymphadenopathy. During the early phase of COVID-19 disease, thorax CT shows multiple small plaques and interstitial alterations, evident in the lung is periphery, further worsens to bilateral multiple ground-glass opacity and/or infiltrating shadows. Pulmonary consolidation may happen in severe cases and pleural effusion is infrequently observed [16]. Pathologic lung CT

imaging has also been used to identify COVID-19 in suspected and/or asymptomatic cases with negative RT-PCR; many of cases have positive PCR when they are repeated [24].

Treatment

1- Supportive Therapy

The first step is to confirm sufficient isolation to stop spread to healthcare staff and other individuals. Suspected cases and confirmed patients should be isolated in a self-isolated at homes or single room subsequent to the doctors' advice. Critical patients should be admitted to ICU immediately. The common strategies involve bed rest, supplying enough calories and water consumption, sustaining water-electrolyte balance and homeostasis, scrutinizing vital signs and oxygen saturation, maintaining airway unobstructed and supplementing oxygen when needed [16].

2- Symptomatic Therapy

The mild disease should be controlled at home by advising about the dangerous signs. The standard approach involves continuing nutrition, hydration and control fever and cough. If a patient has a high temperature > 38.5°C with noticeable distress, bodily cooling or antipyretic, medicine therapy would be given [16]. In hypoxic individuals, oxygen therapy through nasal prongs, face mask, high flow nasal cannula or non-invasive ventilation may be required. Mechanical ventilation and even extra corporeal membrane oxygen (ECMO) treatment might be necessary. Children who go through non-invasive mechanical ventilation for two hours without any progress, or cannot put up with non-invasive ventilation, with augmented airway secretions, severe cough, or hemodynamic unpredictability, should rapidly undergo mechanical ventilation. If required, prone position ventilation, pulmonary recruitment, or ECMO can be implemented [25].

3- Antiviral Therapy

a-Lopinavir-ritonavir (combined protease inhibitor) This methods has been used for HIV infection therapy. The combined protease inhibitor has shown to have an effect on the SARS infection in vitro [26]. In a study, including five cases treated with lopinavir-ritonavir, two cases worsened and three cases recover; four cases of them had gastrointestinal side effects [2]. The combined protease inhibitor has been currently used in treatment of patients with SARS, but its efficacy and safety need to be proved [27].

b- Ribavirin: In study was conducted about SARS, the cases treated with lopinavir-ritonavir with ribavirin had best results when compared to the cases treated with ribavirin only [28].

c- Remdesivir: Many clinical trials are ongoing to assess the supportive use of remdesivir efficacy in severe COVID-19 infection however, the clinical effects of remdesivir on COVID-19 still unidentified. There is anecdotal practice with the utilization of remdesivir, a wide spectrum anti-RNA medication previously used for Ebola in COVID-19 treatment [29].

Prevention

At this time, there is no such a complete guidance to prevent the spread of coronavirus; however, there are some guidelines were presented by the European Centre for Disease Prevention and Control (ECDC) and WHO. Because many studies was presented evidence about human to human transmission of coronavirus from Wuhan, china. Another study demonstrated about airborne transmission of virus while no one was providing the strong evidence. As the lack of transmission evidence health professionals were not able to provide prevention guidelines. According to WHO, some guidelines were published such as separate the infected patient at single room from other family member, and airborne precaution. (ECDC) published an

information leaflet, which has a number of guidelines regarding the prevention of COVID-19 including avoid contact with sick person with a cough, avoid visiting markets, wash your hands with water and soap, use disinfectant solutions before eating or after any contact with animals and after using toilet, and avoid contact with animals, their excretions [18, 24].

Vaccination

The supportive therapy is the only treatment followed by specialist doctors. The supportive therapy includes mechanical ventilation as a respiratory support, maintenance of patient hydration, administration of antipyretic and analgesic and uses of antibiotic in bacterial infections. Some research reported that interferon alpha and ribavirin have offered synergetic effects in the early stage of administration. On the other hand, some studies claimed that mycophenolic acid as monotherapy [22].

There are several steps should be taken to avoid coronaviruses infection, including:

1. Avoiding overexertion, avoiding smoking.
2. Drinking enough water
3. Taking ibuprofen, acetaminophen or naproxen for fever and pain
4. Using a clean humidifier
5. Standard recommendations to prevent spread of coronaviruses: It include good hand washing, covering nose and mouth when coughing and sneezing, avoid direct contact with anyone showing symptoms of respiratory infections.

Conclusion

Corona virus is transmitted from human to human via airborne droplets by sneezing, coughing and kissing. Corona virus may be transmitted via pet such as cat, cow, dog. As per WHO guidelines avoid the direct contact with sick people and also avoid public places

such as markets. Besides testing for other respiratory viral pathogens, a nasopharyngeal swab should be sent for RT-PCR testing. There are no antibiotics to treatment of coronavirus. Management consists of home care, which is likely for mild cases of the disease that can be sufficiently isolated. To decrease the danger of spread coronaviruses in society, people should be advised to carry out respiratory hygiene, good hands washing and keep away from crowds and contact with sick persons.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020). Clinical features of patientsinfected with 2019 novel coronavirus in Wuhan, China. Lancet.

2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al.(2020). A pneumonia outbreakassociated with a new coronavirus of probable bat origin. Nature.

3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. (2020). China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China. N Engl J Med؛ 382(8): 727–33.

4. National Health Commission of the People's Republic of China.(2020). New coronavirus cases rise to 571 in Chinese mainland. Available from: URL: http://en.nhc.gov.cn/2020-01/23/c_76004.htm.

5. World Health Organization. (2020). Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. Availabl from: URL: https:// www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020.

6. Luk H. K., Li X., Fung J., Lau S. K., Woo P. C.(2019). (Molecular epidemiology, evolution and phylogeny of SARS coronavirus. Infection, Genetics and Evolution, 71: 21-30.

7. Imperial College London. Report 2.(2020). estimating the potential total number of novel coronavirus cases in Wuhan City, China. Jan. disease-analysis/news--wuhan-coronavirus.

8. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al.(2020). Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. N Engl J Med; 382(10): 970–1.

9. Kampf G, Todt D, Pfaender S, Steinmann E.(2020). Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect; 104(3): 246–51.

10. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-2019). February 16-24, 2020. http://www.who.int/docs/default- source/coronaviruse/who-china-joint-mission-on-covid-19-finalreport.

11. Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, et al. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep 2020; 69(9): 245–6.

12. Hughes J, Wilson M, Luby S, Gurley E, Hossain M. (2009). Transmission of human infec-tion with Nipah virus. Clin Infect Dis;49(11):1743–8.

13. Yu W, Tang G, Zhang L, Corlett R. (2020). Decoding the evolution and transmissionsof the novel pneumonia coronavirus (SARS-CoV-2) using whole genomic data. China Xiv 2020. Preprint.

14. .Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al.(2020). A Novel Coronavirus from Patients with Pneumonia in China, 2019. New England Journal of Medicine

15. .Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. (2020) Afamilial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet.

16. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al.(2020).Diagnosis، treatment, and prevention of 2019 novel coronavirus infection in children:experts' consensus statement. World J Pediatr.Fes12519-020-00343-7.

17. Dong X, Cao YY, Lu XX, Zhang JJ, Du H, Yan YQ, et al.(2020) Eleven Faces of Coronavirus Disease 2019. Allergy. 2020 Mar 20. doi: 10.1111/ all.14289.

18. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al.(2020). SARSCoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med; 382(12): 1177–9.

19. Interim guidelines for collecting, handling, and testing clinical specimens from persons under investigation (PUIs) for coronavirus disease 2019 (COVID-19). Available from: URL: www.cdc.gov/ coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html. Accessed, March 15, 2020.

20. Tang YW, Schmitz JE, Persing DH, Stratton CW. The Laboratory Diagnosis of COVID 19 infection: Current issues and challenges. J Clin Microbiol. 2020 Apr 3. pii: JCM.00512-20. doi: 10.1128/ JCM.00512-20.

21. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al.(2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet; 395(10223): 497–506.

22. Zhou M, Zhang X, Qu J.(2020). Coronavirus disease 2019 (COVID-19): a clinical update. Front Med. 2020 Apr 2. doi: 10.1007/s11684-020- 0767-8.

23. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al.(2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395(10223): 507–13.

24. Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, et al.(2020). Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology; 295(1): 22–3.
25. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al.(2020). Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA. doi: 10.1001/jama.2020.4783.
26. Chan JF, Yao Y, Yeung ML, Deng W, Bao L, Jia L, et al.(2015). Treatment with Lopinavir/ Ritonavir or interferon-β1b improves outcome of MERS-CoV infection in a nonhuman primate model of common marmoset. J Infect Dis; 212(12): 1904–13.
27. Lim J, Jeon S, Shin HY, Kim MJ, Seong YM, Lee WJ, et al.(2020). Case of the Index Patient Who Caused Tertiary Transmission of COVID-19 Infection in Korea: the Application of Lopinavir/ Ritonavir for the Treatment of COVID-19 Infected Pneumonia Monitored by Quantitative RT-PCR. J Korean Med Sci; 35(6): e79.
28. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, et al.(2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. Mil Med Res; 7(1): 11.
29. Cao YC, Deng QX, Dai SX. Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. Travel Med Infect Dis. 2020 Apr 2:101647. doi: 10.1016/j. tmaid.2020.101647.

The prevalence and Risk Factors of Obesity in Children Attending Al-Kindy Obesity Unit in Baghdad

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Abstract

Background: Childhood obesity is increasing in frequency worldwide with including developing countries. We tried to assess the prevalence of overweight and obesity with associated risk factors in obese children visiting Al-Kindy Obesity Unit.

Methods: Throughout a period started in December 1, 2019 to February 29, 2020 in Baghdad, 109 children were randomly involved, 69 (63.3%) girls and 40 (36.7%) boys. Body mass index was evaluated in front of standard tables. A questionnaire was built to gather suspected risk factors.

Results: 8 (7.3%) of our sample were overweight [1 (2.5%) boy and 7 (10.1%) girls] and 101 (92.7 %) of our sample were obese [39 (97.5%) boys and 62 (89.9%) girls]. Significant associations were found between overweight and health education, sleep, physical activity, snacks and TV watching.

Conclusion: Obesity was more frequently encountered than overweight in children with (heavy weights) who seek help visiting obesity units. Unbalanced dietary habits, sedentary lifestyle and spending more hours on watching TV are important risk factors.

Introduction

Obesity could be identified as a condition of excessive fat deposition in adipose tissue, affecting body health [1]. World Health Organization (WHO) depends on ≥ 30 body mass index (BMI) to indicate obesity [2]. The problem of obesity becomes a major health issue throughout the world [1], leading to higher chances of non-communicable diseases (NCD) [3, 4]. Higher weight is linked to various disease status not limited to central nervous and cardiovascular systems, including breathing abnormalities during sleep, hypertension, malignancy, and diabetes. [5-10] Published papers in our part of the world (Middle East) rang the alarm of excessive weight in our population of different age groups with more than half of total mortality annually due to NCD. [3,4] Globalization is well represented in obesity when both developed and developing countries are affected with major public health threats. [11-13] Owing to the already limited resources of developing world, NCD due to obesity in the community has a significant burden on whole health system which might be greatly improved with even mild to moderate weight modification. [14].

Objectives to assess the prevalence for childhood obesity types in obese patients and associated risk factors.

Patients and Methods

A cross sectional study was performed recruiting randomly selected 109 obese children whom visited Al-Kindy Obesity Unit at Al-Kindy College of Medicine starting from December 1, 2019 to February 29, 2020.

All patients or their care givers who couldn't answer one or more information in the table was excluded from our study. BMI was defined as weight (kg)/ height (m^2). [1] The following criteria for age- and gender-specific body mass index (BMI percentile) has been applied to diagnose childhood obesity as shown in the following table [15], any

child who failed to reach 85th percentile of BMI was excluded from this study.

Table 1: Variables used in the questionnaire

From patients	From files in obesity unit
1-name 2-age 3-gender 4-resident 5-physical activity (exercise, walk to school, playing) 6-time of watching (tv, internet, gaming) 7-time of sleeping 8-dietry habit (meals, snacks) 9-family education (healthy food)	1-weight (in kg) 2-height (in cm) 3-overweight in family (mother, father, brothers)

Table 2: the criteria for age- and gender-specific body mass index (BMI percentile)

Weight Status Category	Percentile Range
Underweight	Less than the 5th percentile
Normal or Healthy Weight	5th percentile to less than the 85th percentile
Overweight	85th to less than the 95th percentile
Obese	Equal to or greater than the 95th percentile

Results

In this study 109 patients including 69 (63.3%) girls and 40 (36.7%) boys were assessed. Mean age of the patients was 9.8±2.9 (3-15) years. Out of the studied patients 8 (7.3%) of them were overweight [1 (2.5%) boy and 7 (10.1%) girls] and 101 (92.7 %) of them were obese [39 (97.5%) boys and 62 (89.9%) girls] (Figure1). Females had higher overweight prevalence without touching significance (p= 0.143)

Table (3) demonstrates the correlation between BMI and physical activity, watching TV, sleep hours and snack each day. The correlation test measures the strength of association between two variables and the direction of the relationship. for example, there is a strong association between BMI and sleep hours according to this test (p value=0.000) and the degree of association is (r=.521) which means that there is a strong positive linear association between BMI and sleep hours.

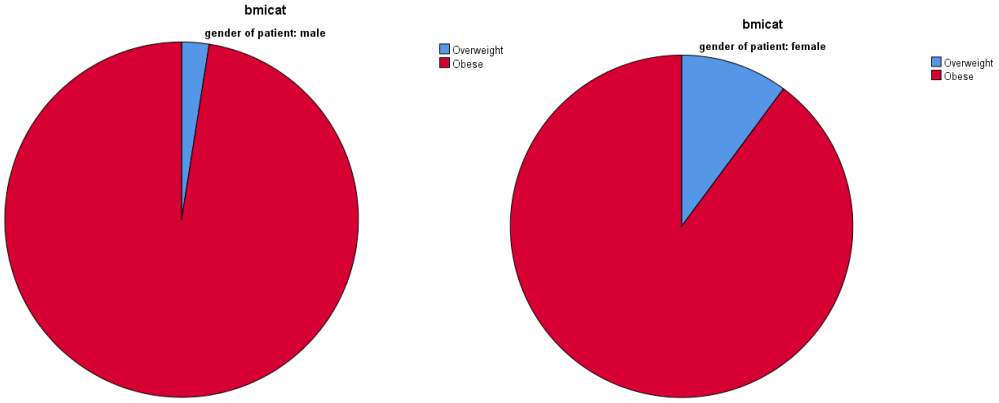

Figure (1) prevalence of overweight and obesity in both male (in the left) and female (in the right).

Table 3: Correlation between BMI and certain risk factors

Correlations

		BMI	physical activity	watching Tv	sleep hours	snacks each day
BMI	Pearson Correlation	1	-.618**	.521**	-.647**	.754**
	Sig. (2-tailed)		.000	.000	.000	.000
	N	109	109	109	109	109

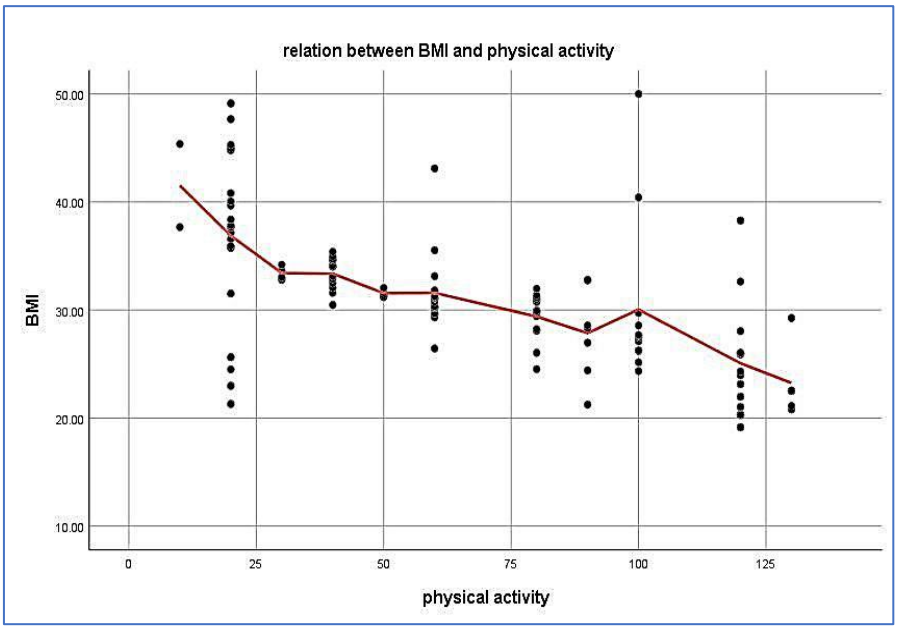

Figure (2): demonstrates the significant inverse association between BMI and physical activity according to the probability value in the correlation test(p=0.000) in table (2).

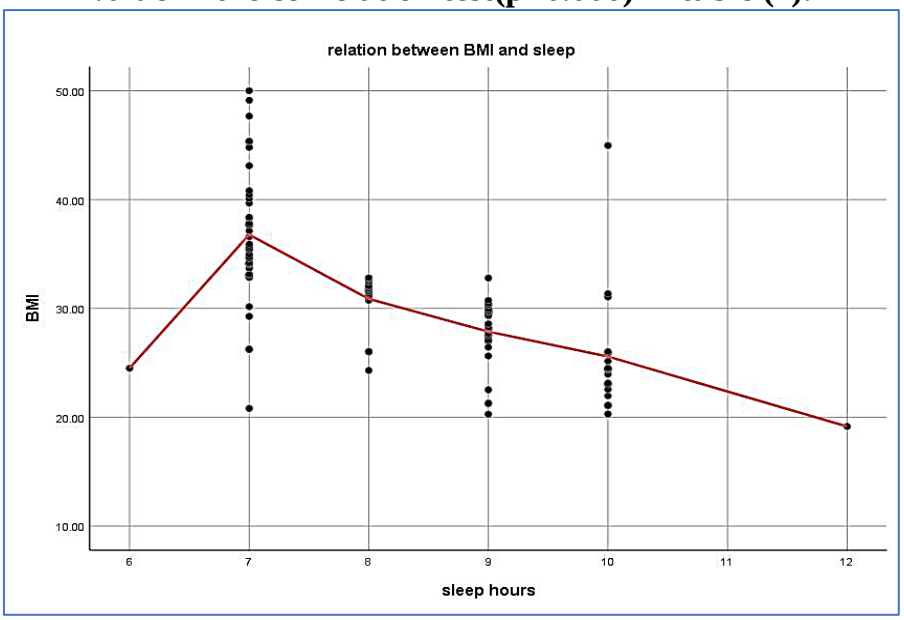

Figure (3): the significant inverse association between BMI and hours of sleep according to the probability value in the correlation test (p=0.000) in table (2).

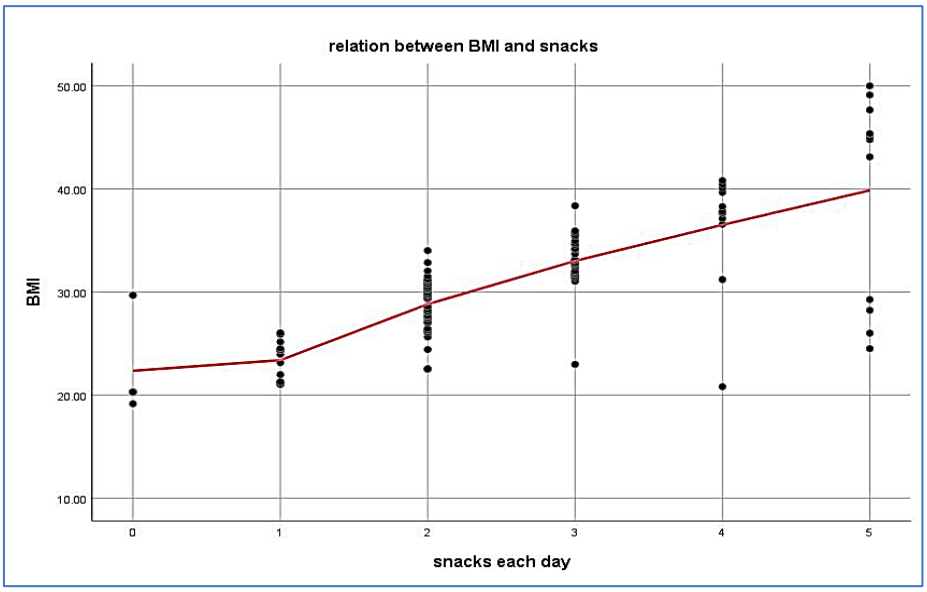

Figure (4): demonstrates the significant linear association between number of snacks each day and BMI according to the probability value in the correlation test(p=0.000) in table (2).

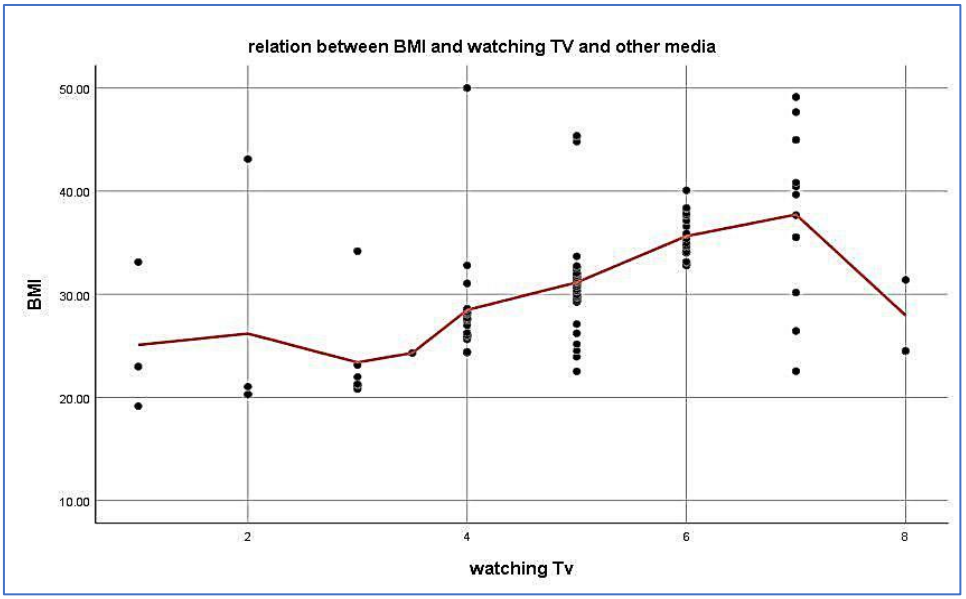

Figure (5): demonstrates the linear significant association between BMI and hours of watching TV and other media each day according to probability value in correlation test (p=0.000) in table (2).

In our statistical analysis, we also did the Pearson chi-square tests to determine if there any association between the BMI and family health education. We found a strong association between them (p value=0.000) and (X=19.01) as the degree of association. The test also showed that there is no association between BMI and family obesity (p= 0.622)

Discussion

The population of Baghdad, as of 2014, is approximately 7,665,292 making it the largest city in Iraq. [16] This study showed an overweight prevalence of (7.3%) which was similar to what have been found by other scientists in England and Scotland (5.4%, and 6.4%, respectively). [17] Our results revealed that weight is increasing with increasing age, in line with other previous findings. [18] Prevalence of overweight in our sample had higher female:male ratio [1 (2.5%) of boys and 7 (10.1%) of girls] but the difference wasn't statistically significant. A similar result was found in Babil governorate in which 8300 students were chosen randomly from 20 primary schools. [19]
Education status of parents of our patients had a significant link with BMI of their children. The higher parental education level the lower childhood weight. This may reflect the important role of community-awareness of parents to protect their children from higher weight gain and avoid possible risk factors. This was agreed by some workers [20], but denied by others. [21] During recent years, a sedentary life style was evident worldwide and affecting various nations. The invasion of electronic materials has changed the world. The American Academy of Pediatrics suggests one- or two-hours' limit of television for children, and completely discourage that for children below two years. [22, 23]

A study done in United States showed that one hour of television watching was associated with lower obesity incidence, in contrast to four hours of watching. [24] In the current study, mean hours of

watching TV and using of digital media (computers, video games) was 4.9±1.4 (1-8) hours daily which is in great agreement with the above findings in United States. According to WHO, individuals of 5–17 years` age should have at least one hour of moderate- to vigorous-intensity physical activity daily. [25]

The study showed an average of 67.7±36.6 (10-130) minutes daily of physical activity during (sport, play, school). Sleep is important for growth of children and adolescents due to wonderful diurnal hormonal release which has a great impact on growth and maturation of body cells [26]. Little sleeping time may affect levels of different growth hormones such as cortisol, ghrelin, leptin, growth hormone, leptin, and insulin leading to higher weight accumulation. [27-29]

The patients had 8.3±1.2 (6-12) hours of sleep as a mean, which was near to previous publishing. [30] It is well-known that obesity results when an imbalance was evident between energy intake as calories and calories needed daily. [31] As a recently noticed habit, snacks and food intake between major meals are a recognized factor of excessive weight gain. [32]

The patients had a mean of 2.62±1.3 (0-5) snacks daily. However; most of overweight childhood population (93%) in a previous local study had the habit of snacks consumption.

Conclusion: Obesity prevalence and risk factors in our children sample was similar to other parts of the world.

References

[1] WHO Obesity: preventing and managing the global epidemic [Internet]. Who.int. 2018 [cited November 17, 2020]. Available from: http://www.who.int/nutrition/publications/obesity/ WHO_TRS_894/en/

[2] D. W. Haslam and W. P. T. James, “Obesity”, The Lancet, vol. 366, no. 9492, pp. 1197–1209, 2005.

[3] Musaiger AO. Overweight and obesity in the Eastern Mediterranean Region: can we control it? East Mediterr Health J. 2004; 10(6):789-93.
[4] Sibai AM, Nasreddine L, Mokdad AH, Adra N, Tabet M, Hwalla N. Nutrition transition and cardiovascular disease risk factors in Middle East and North Africa countries: reviewing the evidence. Annals of Nutrition and Metabolism. 2010; 57(3-4):193-203.
[5] Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ, Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. The Lancet. 2002 Nov 2; 360(9343):1347-60.
[6] Al-Momen HH, Shallal HH, Abbas SS. Outcome Prediction of Acute Lymphoblastic Leukemia Using Nutritional Backgrounds. Age (year);1(10):18.
[7] Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation. 1983 May 1;67 (5):968-77.
[8] Poirier P, Eckel RH. Obesity and cardiovascular disease. Current atherosclerosis reports. 2002 Nov 1;4(6):448-53.
[9] Ceschi M, Gutzwiller F, Moch H, Eichholzer M, Probst-Hensch NM. Epidemiology and pathophysiology of obesity as a cause of cancer. Swiss medical weekly. 2007 Jan 27;137(3/4):50.
[10] Al-Momen H, Majeed BA, Obed AA, Hussein MJ. International Journal of Research in Pharmaceutical Sciences.
[11] Malina RM, Katzmarzyk PT. Validity of the body mass index as an indicator of the risk and presence of overweight in adolescents. The American journal of clinical nutrition. 1999 Jul 1; 70(1): 131S-6S.
[12] Garrow JS. Obesity and related diseases. Churchill Livingstone; 1988:329.

[13] Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. Bmj. 2000 May 6; 320 (7244): 1240.
[14] Nguyen DM, El-Serag HB. The epidemiology of obesity. Gastroenterology Clinics. 2010 Mar 1; 39(1):1-7.
[15] About Child & Teen BMI | Healthy Weight | CDC [Internet]. Cdc.gov. 2018 [cited November 17, 2020]. Available from: https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html
[16] 2. [Internet]. Cosit.gov.iq. 2018 [cited November 17, 2020]. Available from: http://www.cosit.gov.iq/AAS2016/ population/ population(8).htm
[17] Chinn S, Rona RJ. Prevalence and trends in overweight and obesity in three cross sectional studies of British children, 1974-94. Bmj. 2001 Jan 6; 322(7277):24-6
[18]. Kinra S, Nelder RP, Lewendon GJ. Deprivation and childhood obesity: a cross sectional study of 20 973 children in Plymouth, United Kingdom. Journal of Epidemiology & Community Health. 2000 Jun 1;54(6):456-60.
[19] Lafta RK, Kadhim MJ. Childhood obesity in Iraq: prevalence and possible risk factors. Annals of Saudi medicine. 2005;25(5):389-93.
[20] Fredriks AM, Van Buuren S, Burgmeijer RJ, Meulmeester JF, Beuker RJ, Brugman E, Roede MJ, Verloove-Vanhorick SP, Wit JM. Continuing positive secular growth change in The Netherlands 1955–1997. Pediatric research. 2000 Mar;47(3):316.
[21] Tanasescu M, Ferris AM, Himmelgreen DA, Rodriguez N, Pérez-Escamilla R. Biobehavioral factors are associated with obesity in Puerto Rican children. The Journal of nutrition. 2000 Jul 1;130(7):1734-42.
[22] Schmidt ME, Rich M, Rifas-Shiman SL, Oken E, Taveras EM. Television viewing in infancy and child cognition at 3 years of age in a US cohort. Pediatrics. 2009 Mar 1;123(3): e370-5.
[23] Takeuchi H, Taki Y, Hashizume H, Asano K, Asano M, Sassa Y, Yokota S, Kotozaki Y, Nouchi R, Kawashima R. The impact of

television viewing on brain structures: cross-sectional and longitudinal analyses. Cerebral cortex. 2015 May 1;25 (5):1188-97.
[24] Kline S. Countering children's sedentary lifestyles: an evaluative study of a media-risk education approach. Childhood. 2005 May;12(2):239-58.
[25] WHO | Physical activity and young people [Internet]. Who.int. 2018 [cited November 17, 2020]. Available from: http://www.who.int/dietphysicalactivity/factsheet_young_people/en/
[26] Mindell JA, Owens JA, Carskadon MA. Developmental features of sleep. Child Adolesc Psychiatr Clin N Am 1999; 8: 695–725.
[27] Spiegel K, Leproult R, L'Hermite-Balériaux M, Copinschi G, Penev PD, Van Cauter E. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. The Journal of clinical endocrinology & metabolism. 2004 Nov 1;89(11):5762-71.
[28] Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. The lancet. 1999 Oct 23; 354(9188):1435-9.
[29] Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS medicine. 2004 Dec 7;1(3): e62.
[30] Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, Malow BA, Maski K, Nichols C, Quan SF, Rosen CL. Recommended amount of sleep for pediatric populations: a consensus statement of the American Academy of Sleep Medicine. Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine. 2016 Jun 15;12(6):785.
[31] Nielsen SJ, Siega Riz AM, Popkin BM. Trends in energy intake in US between 1977 and 1996: similar shifts seen across age groups. Obesity. 2002 May 1;10(5):370-8.
[32] Jahns L, Siega-Riz AM, Popkin BM. The increasing prevalence of snacking among US children from 1977 to 1996. The Journal of pediatrics. 2001 Apr 1;138(4):493-8.

Impact of ACE2 Genetic Polymorphisms rs2106809 and rs2074192 on Gender Susceptibility to COVID-19 Infection and Recovery

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Abstract:

Epidemiology studies revealed different sex and age groups have different susceptibility to infection with SARS-CoV2 with males and older age being the most inflicted. There is a clear indication that deaths caused by COVID-19 in males appeared at a higher rate than females across 35 nations. The implication of associated disease risk genes involved in the susceptibility of COVID-19 such as the angiotensin converting enzyme 2 (ACE2) has recently received a good attention due its role in acute lung injury and in mediating SARS-CoV2 entry as a host receptor. Here by analyzing two main genetic polymorphisms of ACE2 (rs2106809 and rs2074192), we found that there was a differential genotype distribution between males and females in various global population whereas mutant variants were common in males compared to unchanged variants among females which may reflect differences in gender susceptibility to infection with SARS-CoV2.

Keywords: COVID-19, SARS-COV2, gene polymorphism, gender, ACE2

Introduction

Coronavirus is a large family of viruses that cause illnesses ranging from the common cold to severe pneumonia, such as SARS1and Middle East Respiratory Syndrome (MERS).[2] SARS-CoV-2 was first identified in Wuhan, China, by the Chinese Center for Disease Control and Prevention (CDC).[3] Both epidemiological4 and clinical5 features of patients with COVID-19 have recently been reported. However, little data on the effect of genetic polymorphisms of ACE2 on gender susceptibility to infection and rate of recovery of COVID-19.

As indicated by sex-disaggregated information incorporated by worldwide scientists, there is a clear indication that coronavirus-related deaths with males appeared at a higher rate than females across 35 nations (Worldwide Health 50/50). For example, the extent of deaths among people adds up to·13.3\7.4 in Italy, 4.7\2.8 in China, 8.4\4.7 in Spain, 10.6\6.6 in The Netherlands), and 4.0\1.7 in Ireland (https://globalhealth5050. org/covid19/#1586248980572-3839d9fe-3b88 and https:// fivethirtyeight.com/ features/ why-are-more-men-than-women-dying-of-covid-19/). In addition, the ratio of males who were at a higher risk to infection with COVID-19 by 70.3 compared to 29.3 in females.[1] Gender equality index finding revealed also that women are at a greater risk of infection than males due to multiple factors: women commute via public transport, do grocery shopping and sometime dominate many professions Epidemiology studies revealed different sex and age groups have different susceptibility to infection with SARS-CoV2 with males and older age being the most inflicted. [6, 7]

The implication of associated disease risk genes involved in the susceptibility of COVID-19 such as the angiotensin converting enzyme 2 (ACE2) has recently received a good attention due its role in acute lung injury.[8] The genetic variants of ACE2 showed to be correlated with circulating angiotensin-(1-7) levels in hypertensive females.

ACE2 was shown to work as a host receptor for SARS-CoV2.[9] The ACE2 gene exhibited a high degree of genetic polymorphisms among different population around the globe which may influence the susceptibility to infection and/or disease progression to COVID-19. In this regard, this study sought to explore whether the genetic polymorphism in the ACE2 gene, particularly rs2106809 and rs2074192 would explain the genetic differences between males and females toward infection with SARS-CoV2 in various parts of the world.

Study Design

This study attempted to provide an answer for the variable infection and mortality rates of the SARS-CoV2 between males and females worldwide. It is not yet known whether this differential rate of susceptibility between genders to infection/mortality of SARS-CoV2 is attributed to the genetic variants of the main host receptor ACE2 in various ethnic populations. Therefore, two main genetic polymorphisms rs2106809 and rs2074192 were screened and analysed using previously published public data amongst selected populations.

Results and Discussion

By analyzing public data, it was found that the two SNPs (rs2106809 and rs2074192) expressed at variable proportions among different ethnic population around the world. A summary of these findings was outlined in Table 1. The prevalent genotypes of rs2074192 among Caucasian males were almost dominated by TT mutant genotypes whereas TT or CT genotypes were common in females.

Table 1. Genotype distribution of ACE2 (rs2106809 and rs2074192) genetic polymorphisms among different world population

SNP	Reference	Genotype			Male most frequent genotype	Female most frequent genotype	Country	Race
		Wild type	Hetero	Homo mutant				
rs2106809	2	CC M:35.1% F:21.7%	CT M: - F:56.5%	TT M:64% F:50%	TT	CT	Egypt	Middle Eastern
	3	CC M: F:85%	CT M F:10%	TT M: F:5%	NA	CC	India	Asia
rs2074192	4	CC M:57.1% F:34%	CT M: NA F:44.7%	TT M:42.9% F:21.4%	CC/TT	CT	Australia	Caucasian
	5	CC	CT	TT M:24.7% F;43.9%	NA	TT	Canadian	Caucasian
	5	CC	CT	TT M:47 % F:46.8%	TT	TT	Canadian	Caucasian
	11	CC M: - F:38.7%	CT M: - F: 41.1%	TT M: - F:19.8%	NA	CC/CT	China	Asia
	12	CC M: 61% F:41%	CT M: - F:41%	TT M:39% F:17%	CC/TT	CC/ CT	China	Asia

Abbreviations: NA, not available.

On the other hand, the genotype trend was changed in the Asian female population as CC or CT (no mutant genotypes were observed) with no considerable difference among males than those observed with the Caucasian. Similar pattern for the rs2106809 genotypes particularly among females in the Middle East and India. Taken together for both genetic polymorphisms, it appeared that males had mutant genotype compared to either wild or heterozygous mutant in females. Considering the limitation of sample size number, these data may suggest that the mutant genotype among males could contribute to the severity of infection in males compared to females around the world but the absence of such variants in females may explain the low infectivity/mortality rate seen among them. In a previous study conducted in Hong Kong during the SARS infection it was found that the cases of SARS-CoV1 fatality was 13.2% for females and males

were 21.9 % [10].The risk value of mortality estimate of 1.66 for males compared with females.

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References

1. Jin, J. M., et al., Gender differences in patients with COVID-19: Focus on severity and mortality. Frontiers in Public Health, 2020. 8: p. 152.

2. egyptian, s.t.h.c.i., association of ace and ace2 genes polymorphisms with susceptibility to hepatocellular carcinoma in egyptian hcv patients. journal of global biosciences, 2015. 4(5): p. 2393-2403.

3. Patnaik, M., et al., Association of angiotensin-converting enzyme and angiotensin-converting enzyme-2 gene polymorphisms with

essential hypertension in the population of Odisha, India. Annals of human biology, 2014. 41(2): p. 145-152.
4. Patel, S.K., et al., Association of ACE2 genetic variants with blood pressure, left ventricular mass, and cardiac function in Caucasians with type 2 diabetes. American journal of hypertension, 2012. 25(2): p. 216-222.
5. Malard, L., et al., The association between the angiotensin-converting enzyme-2 gene and blood pressure in a cohort study of adolescents. BMC medical genetics, 2013. 14(1): p. 117.
6. Chen, Y., Q. Liu, and D. Guo, Emerging coronaviruses: genome structure, replication, and pathogenesis. Journal of medical virology, 2020.
7. Chen, N., et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet, 2020. 395 (10223): p. 507-513.
8. Imai, Y., et al., Angiotensin-converting enzyme 2 protects from severe acute lung failure. Nature, 2005. 436(7047): p. 112-116.
9. Cao, Y., et al., Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. Cell Discovery, 2020. 6(1): p. 1-4.
10. Karlberg, J., D. Chong, and W. Lai, Do men have a higher case fatality rate of severe acute respiratory syndrome than women do? American journal of epidemiology, 2004. 159(3): p. 229-231.
11. Chen, Y., et al., Relationship between genetic variants of ACE 2 gene and circulating levels of ACE 2 and its metabolites. Journal of clinical pharmacy and therapeutics, 2018. 43(2): p. 189-195.
12. Meng, N., et al., Association of polymorphisms of angiotensin I converting enzyme 2 with retinopathy in type 2 diabetes mellitus among Chinese individuals. Eye, 2015. 29(2): p. 266-271.

Pharmacovigilance: Current Implications and Future Perspectives

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Pharmacology is a broad discipline, incorporating not only drug actions, therapeutics and clinical management, but also drug safety issues. Drug safety and pharmacovigilance is a key component of clinical practice, research and drug regulation. Adverse drug reactions (ADRs) have been defined by the World Health Organization (WHO) as: "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function". [1] These ADRs have led to increase in morbidity and mortality in patients and community, hence we need to continuously monitor and analyze the safety of medicine in order to minimize the risks. Thus, pharmacovigilance was started globally for continuous monitoring of unwanted and other safety – related aspects of marketed drugs. According to WHO, Pharmacovigilance (PV) is defined as "the science and activities related to the detection, assessment, understanding and prevention of adverse drug effects or any other possible drug-related problems. [2]

The prime activity of the Pharmacovigilance is to collect, collate and analyse data on adverse drug reactions to arrive at an inference to recommend regulatory interventions, besides communicating associated risks to healthcare professionals. Each member country under WHO has developed its own robust system of collecting ADR data in a systematic manner from hospitals, clinicians, health professionals, pharmaceutical companies and even patients which is

assembled and analysed by the National Coordinating Centre (NCC) of the country and then forwarded to WHO Collaborating Centre for International Drug Monitoring located at Uppsala, Sweden known as Uppsala Monitoring Centre (UMC). UMC was started in 1978 and at present has more than 100 member countries. The reports are collected in form of ICSRs (individual case safety reports) from healthcare providers and patients and entered in database VigiFlow, maintained by NCC of the country. UMC maintains a global individual case safety report database known as VigiBase on behalf of the WHO. [3]

VigiAccess is a web-based application which helps in accessing information about ADR of drugs and vaccine globally. VigiLyze is a signal detection and management system that NCCs can access and use the domestic, local or global data for quantitative signal detection. [4]

Applications of Pharmacovigilance is in varied arenas. In clinical trials, Data Safety Monitoring Board (DSMB) continuously monitors and reports the ADRs encountered by the new product. In Postmarketing surveillance (Phase IV) safety of drugs is evaluated on a large scale in a wide population. The ADR data collated and analysed by NCC of a country leads to withdrawal of drug from market, issue black box warnings, drug alerts or signal generation which would help in formulating and amending national drug policies.

In order to distinguish between an adverse event (AE) and an adverse drug reaction causality assessment has to be done as an AE may not necessarily have a causal relationship with the drug exposure or treatment, which is usually present in case of an ADR. Causality assessment is the systematic review of individual case safety report to determine the relationship between adverse event & causal drug. It attempts to find out the exact drug responsible for causing drug reaction and is an important and challenging part of pharmacovigilance. There are many scales used for causality assessment but the most reliable, reproducible and widely used are WHO- UMC & Naranjo

Probability Scale. These scales are internationally acceptable as they are in a structured and standardized format, easy to use, less complex and less time consuming. The assessment Criteria are time relationship between drug administration & event, Known ADR mentioned in literature based on pharmacological characteristics, event cannot be explained by a medical condition and exclusion of other causes, dechallenge-on withdrawal of drug the reaction subsides and rechallenge i.e., re-administration of drug leading to reappearance of reaction which is usually not performed under normal circumstances though it may occur unknowingly by chance. [5, 6]

The events are categorized as Certain when all 5 criteria are fulfilled, Probable when 4 criteria are fulfilled excluding rechallenge, Possible only when time relation is present and it could also be explained by other disease and information on drug withdrawal lacking or unclear, Unlikely when time relation is also doubtful and questionable (but not impossible) and Conditional /Unclassified when more data needed for proper assessment. Pharmacovigilance not only includes side effects by drugs or medicines only but reactions caused by vaccines, herbal drugs and medical devices are also included. Though most vaccines used are safe and effective but may sometimes lead to mild, moderate or serious reactions, an unfavourable symptom or an abnormal laboratory finding. These are known as adverse events following immunization (AEFIs) which may or may not have a causal relationship with vaccine administration. AEFIs may include common symptoms classified as minor, like low grade fever, local pain and swelling or severe like pain and swelling which spreads beyond the nearest joint or high-grade fever and serious AEFIs like anaphylactic reactions or other conditions requiring hospitalization or leading to disability or death.

In current decade extensive use of herbal medicines, nutraceuticals, vitamins, dietary and food supplements, traditional medicines, though

are perceived to be safe may also produce adverse drug reactions or herb drug interactions some of which have been reported to be serious and fatal. The major challenge in herbal pharmacovigilance is easy availability of these products as over the counter (OTC) medicines, self-administration by majority of population, misidentification of herbal constituents, maintenance of quality standards and proving causal association of reaction with the intake of such products. Pharmacovigilance tools, such as spontaneous reporting, prescription-event monitoring and the use of computerized health record databases, are currently being used for evaluating the safety of herbal medicines although modified tools are being developed. Recently the FDA has shown concern about ADR caused by medical devices and has launched the Medical Device Reporting (MDR) as a tool to monitor device performance and detect potential device-related safety issues for consumer benefits. Major countries have specifically defined medical devices, but Global Harmonization Task Force (GHTF) has defined a medical device as any instrument, apparatus, machine, appliance, implant, in vitro reagent or calibrator, software, material, or other similar or related article, which is thereby intended to be used by the manufacturer for human beings for the specific purposes of diagnosis, prevention, monitoring, treatment, or alleviation of disease or compensation for an injury, investigation, replacement, modification, or support of the anatomy or of a physiological process, supporting or sustaining life, control of conception, disinfection of medical devices and in vitro examinations. [7] To monitor the ADR caused by any medical devices the Materiovigilance program was launched in many countries to keep a vigil on these devices.

Based on post marketing surveillance and ADR data some drugs were withdrawn from the market in the last two decades. Cerivastatin was withdrawn from the global market in 2001, due to reports of fatal rhabdomyolysis leading to kidney failure. Cisapride, a prokinetic

agent used for the treatment of gastroesophageal reflux disease (GERD) was withdrawn in many countries due to risk of cardiac arrhythmias caused by prolonged QT syndrome. [8] Rosiglitazone, an antidiabetic drug in the thiazolidinedione class exhibited increased risks of heart attacks and death and thus was withdrawn. Rimonabant, an anorectic antiobesity drug that was first approved in Europe in 2006 but was withdrawn from global market in 2008 due to psychiatric side effects like depressive disorder, mood alterations and suicidal ideation. Lumiracoxib is a COX-2 selective inhibitor nonsteroidal anti-inflammatory drug, was withdrawn from the market in 2007 in Australia following serious liver adverse events followed by withdrawal in several European countries. The list of withdrawn drugs based on ADR reports is exhaustive which indicates a robust global pharmacovigilance system.

Pharmacovigilance plays a crucial role in monitoring drug safety but it is faced with innumerable challenges like exposure of medicines to a global population, irrational drug usage, medication errors, conflict of interest with the pharmaceutical industry, communication gaps between health professional bodies and public and data processing of huge collected data. All these activities may be limited by requirement of huge manpower, time and cost, thus may require a new technology. Artificial intelligence (AI) technologies are one such application which may facilitate ICSR processing, decision making, tracking the risk factors and information dissemination thereby improving accuracy and quality of reports and curtailing the cost. [9] AI strategies are still in infancy stage and more research and collaborations are needed for future advancement in the field of pharmacovigilance. Its application in PV has the potential to further protect the health and safety of patients and other healthcare consumers.

References

1. World Health Organization. International Drug Monitoring: The Role of National Centres, Report of a WHO Meeting [Held in Geneva from 20 to 25 September 1971]. World Health Organization.

2. World Health Organization. WHO Operational Package for Assessing, Monitoring and Evaluating Country Pharmaceutical Situations: Guide for Coordinators and Data Collectors. Geneva: World Health Organization; 2007.

3. Lindquist M. Vigibase, the WHO Global ICSR Database System: Basic Facts. Drug Information Journal, 2008, 42:409–419.

4. UMC WHO [Internet] [Last modified on 2018 Oct 11]. Available from: https://www.who-umc.org/about-us/who-we-are/

5. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981; 30:239–45.

6. The use of the WHO–UMC system for standardized case causality assessment. Accessed from:http://www.WHO-UMC.org/graphics/4409.pdf (last accessed on 2020 Nov 12)

7. Information document concerning the definition of the term "Medical Device". 2005. May, [Accessed 2020 Oct 14]. http://www.ghtf.org/sg1/sg1-final.html.

8. Qureshi, ZP; Seoane-Vazquez, E; Rodriguez-Monguio, R; Stevenson, KB; Szeinbach, SL (July 2011). "Market withdrawal of new molecular entities approved in the United States from 1980 to 2009". Pharmacoepidemiology and Drug Safety. 20 (7): 772–7.

9. Murali K, Kaur S, Prakash A, et al. Artificial intelligence in pharmacovigilance: Practical utility. Indian J Pharmacol. 2019 Nov-Dec; 51(6): 373–376.

Anticancer, Cytotoxicity and Antimicrobial of Zinc Oxide Nanoparticles

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Abstract.

Zinc oxide nanoparticles (ZnO-NPs) are versatile inorganic metal oxide nanoparticles known widely dueto their wide range of applications. In this study, chemical method was used to prepare ZnO-NPs. The size and shape of the prepared nanomaterial were characterized by Transmission Electron Microscopy (TEM). The average length and diameter of the prepared ZnO-NPs were nearly between 100 nm to 200 nm and 25 nm to 50 nm, respectively. The prepared ZnO-NPs were *in vitro* tested as an anticancer agent toward breast cancer cell lines (MCF-7). The results of MTT assay showed that ZnO-NPs is a promising drug against MCF-7. The prepared ZnO-NPs was also tested as an antimicrobial agent againstgram-negative and gram-positive bacterium. *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) were selected as test bacteria. The antibacterial profile of the prepared ZnO-NPs was also studied with different concentration of ZnO-NPs by different methods such as disc method, well diffusion agar method, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). Moreover, the effect of time with different concentrations of Zn-ONPs on the growth of *E. coli* and *S. aureus* was studied. Five different concentrations of ZnO-NPs were used in order to determine the MIC that includes 15, 10, 5, 2.5, 1, and 0.5 mg/mL. The MIC values were found to be 1 and 0.5 g/m for *E. coli* and *S. aureus*, respectively. The resistivity against gram-positive bacteria was found to be less as compared to that of gram-negative bacteria. Increasing the concentration of ZnO-NPs was

resulted in increasing the antibacterial activity of ZnO-NPs. The antibacterial effect of ZnONPs was time dependent and the effect was gradually.

1. Introduction

Nanoparticles can be defined as a group of materials that have unparalleled characteristics and wide range of applications in various arenas [1-2]. In other words, there are a huge difference in term of properties between nanoparticles and their bulk size counterparts [3-4]. Several materials were classified as safe materials show a toxicity behavior when it turns to nano size particles [5-6]. This phenomenon is basically due to the increasing in which is mainly related to the increasing in surface area and chemically active at nano size scalelevel [7-8]. Increasing the surface area plays an important role asit increases the reactivity with the organic sites that presents in organism cell surface [9].

Now a days, zinc oxide nanoparticles (ZnO-NPs) has become an interesting metal oxide material for researchers due to its remarkable chemical and physical characteristics such as nontoxic nature, high activity as catalysis, good piezoelectric, stable mechanically and chemically, high absorption of radiation, etc. Synthesis of ZnO-NPs can be achieved using several approaches such as controlled precipitation, vapor transport process, micro emulsion synthesis, etc. [10].

Using chemical method to prepare ZnO-NPs has several advantages as compared to other method such as the large surface area and better porosity, which play an important role to increase the possibility to interact with the bioorganic molecules that is found in the viable cell surface [11]. Other advantages of preparation ZnO-NPs by chemical method are simplicity, relatively inexpensive, and can obtain nanoparticles in high crystalline and low dimeter. In general, inorganic

metal oxide nanoparticles and especially ZnO-NPs show a very toxicity selectivity toward bio-systems which make it a considerable option as antimicrobial agent to be used in various applications such as in surgical instruments, curative, diagnosis, and in nano-medication [12]. ZnO-NPs is considered as a great option as an antimicrobial agent due to their great effective to resist strains for pathogen of microbials as well as low toxicity and can provide a resistance toward heat. Moreover, ZnO-NPs offer the essential mineral substances for organism cells and can provide a strong activity when applied even in small amount.

Due to its unique characteristics, it has been used extensively in different areas such as pharmaceutical and cosmetic industries, electro technology industries, rubber industry, textile industries, etc. It has also been investigated to be used in possible applications in medicine. It shows a high degree of selectivity toward cancer cells and it can beat the therapeutic indicators of some traditionally chemotherapeutic drugs [13].

2. Materials and Methods

Different chemicals were used to prepare ZnO-NPs, which were zinc sulphate heptahydrate ($ZnSO_4.7H_2O$ M=287.54 g/mol, Merck), sodium hydroxide (NaOH, M=39.99 g/mol, Sigma Aldrich) and polyvinyl alcohol which was used as a surfactant (PVA, Sigma Aldrich). *Staphylococcus auerus* was derived from NCTC 12493 and *Escherichia coli* was obtained from drinking water sources in south of Iraq. The growth of these microbials was achieved in nutritious solution for 24 h at 37°C under air prior to be the aimed organisms. The density of these isolated strains was set to match the optimum density of 0.5 McFarland standards.

2.1 ZnO-NPs Preparation

ZnO-NPs was prepared by adding 0.01% of PVA solution to 1M of $ZnSO_4.7H_2O$ solution. Then 2M of NaOH was added drop wise to the mixture with continuing stirring for 24 h. After this period, it was noticed a big amount of white powder was participated. Filtration and washing with distilled water for this residue was obtained and the powder was placed in a conventional oven to dry at 100 °C for 6 h. The dried powder then grinded by dome shape grinder and to obtain fine powder and finally it was calcinated under N_2 gas at 450 °C for 3 h.

2.2 Transmission Electron Microscope (TEM)

The structure of the prepared ZnO-NPs as well as the shape and particle size were examined by transmission electron microscopy (TEM). Hitachi H7500 instrument was used for TEM analysis and the voltage was accelerated to 70 kV. The prepared nanoparticles were dispersed in acetone and then a few drops of the mixture were on carbon-coated 400 mesh copper grids.The mesh was left for 10 minutes to dry the acetone at room temperature prior to insert it inside the TEM instrument.

2.3 Anticancer Activity by MTT Assay

The MTT assay was carried out by using 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide in order to investigate the anticancer activity of the prepared ZnO-NPs. Trypsin of cells culture of the breast cancer fibroblast was carried outin addition to setting the number of the cells to be approximately 20,000 cells for 200 µL of the suspension. 200 µL of the diluted cell suspension was added to each well in the microtiter plate, followed by incubation at 37 °C and under 5% of CO_2 gas for 24 h. After that 200 µL of the rested drugs were added to these wells with different test concentrations. Similarly, incubation of these plates was carried out at 37 °C and under 5% of CO_2gas for another 24 h. Then 10% of MTT was added as a reagent to each followed by incubation at 37 °C and under 5% of CO_2 gas for 5 h.

The absorbance of the samples was checked by using microplate reader a wavelength of 570 nm. The cell viability was calculated as follows:

$$\textbf{\textit{Cell vialbility}} = \frac{\textbf{\textit{Test}}}{\textbf{\textit{Control}}} \times \mathbf{100} \ldots (1)$$

2.4 Antibacterial Activity Assay

The antibacterial activity assay of the prepared ZnO-NPs against *E. coli* and *S. aureus* was carried out by suspending ZnO-NPs in sterile normal saline with continues stirring to form a suspension with a ratio of 1000 mg/ml. To assess the toxicity of ZnO-NPs, the test bacteria were vaccinated in nutrient broth medium with a series of ZnO-NPs in a range between 10 to 0.250 mg/ml. The samples were incubated at 37 °C for 24 h and quantified by Colony forming units (cfu).

2.5 Determination of Minimum Inhibitory Concentration

Agar dilution test was used in order to measure MIC and MBC. The targeted bacteria were inoculated on nutritious agar and different concentrations of ZnO-NPs were applied. Quantitation of colony forming unit (cfu) was used to determine the rates growth for the bacteria. The samples that the bacteria did not grow after being incubated was selected. These samples transferred to a new medium that did not have ZnO-NPs after adding 0.1 ml of distilled water.

2.6 Time Dependent Test

The time dependent study was conducted by placing the same amounts of *E. coli* and *S. aureus* in nutritious broth with different concentrations of ZnO-NPs 0.2 ml of both bacteria were distributed on nutrient agar individually with respect of time. The samples were incubated at 37°C for 24 h. 0.1 ml of different cultures was distributed on nutrient agar individually with respect of time. This followed by counting the cfu for each sample well as comparing the cfu of the control sample. All experiments were carried out in triplicate and the average value was acquired.

3. Results and Discussion

Figure 1 shows the TEM image of ZnO-NPs. The ZnO-NPs image revealed that the particles are uniform distributed. The average ZnO-NPs length and diameter of the particles were nearly between 100 nm to 200 nm and 25 nm to 50 nm, respectively. the TEM image of the ZnO-NPs shows that the particles are of sizes of nano scale and in the range 25-50 nm in addition to their spherical shape.

Several advantages can be obtained in conducting in vitro experiments such as simple to perform, time consuming is less and can offer an acceptable range for *in vivo* study. The results of the *in vitro* of the cytotoxicity study were obtained after incubation of the sample for 24 h and using ZnO-NPs with different concentrations within the range between 0.05 to 0.5 mg/mL. It was noticed various phases of cells death at different by applying numerous concentrations of ZnO-NPs [14].

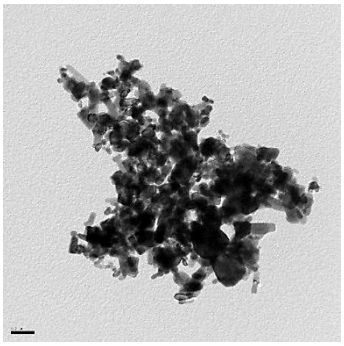

Figure 1. TEM image of the prepared ZnO-NPs

The cytotoxicity results revealed that by using 100 mg/mL of ZnO-NPs, MCF-7 cells were necrotized which indicates that ZnO-NPs toxicity is nearly similar to the traditional camptothecin drug which has a toxicity value of 50 g [15]. The cytotoxic effect of ZnO-NPs on MCF-7 cell is illustrated in Figure 2. The results show a reverse relation between ZnO-NPs concentration and the cell viability. The required concentration of ZnO-NPs to prevent the growing of the cell by 50% was found to be 0.1mg/mL of ZnO-NPs.

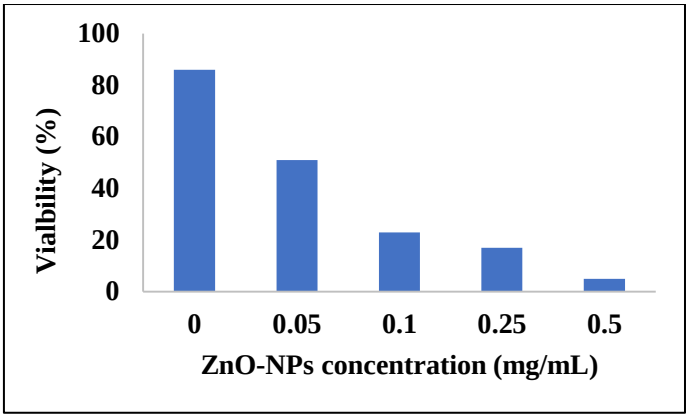

Figure 2. Cell viability of MCF-7 cells calculated by MTT assay. Cells were incubated for 24 h with the ZnO NPs prepared.

Tables 1 and 2 shows the zone of inhibition (ZOI) for *S. areus* and *E.coli*, respectively, of ZnO-NPs by the disc and well diffusion agar methods. The effect of using ZnO-NPs was indicated by the existence of an inhibition zone. It was noticed that when the concentration of ZnO-NPs increased in both methods, the inhibition of growth was also increased, which is in agreement with some other reported studies Rizwan *et al*. [16]. Moreover, the inhibition zone size was varied with the bacteria type, and ZnO-NPs concentrations.

Table 1. Zone of inhibition (ZOI) for S. areus.

ZnO concentration in wells (mg/mL)	ZOI (mm)	ZnO concentration in discs (mg/ml)	ZOI (mm)
15	33	15	30
10	30	10	26
5	28	5	23
2.5	26	2.5	20
1	22	1	17
0.5	0	0.5	0
0	0	0	0

Table 2. Zone of inhibition (ZOI) for E. coli.

ZnO concentration in wells (mg/mL)	ZOI (mm)	ZnO concentration in discs (mg/ml)	ZOI (mm)
15	23	15	42
10	20	10	36
5	17	5	30
2.5	15	2.5	20
1	0	1	0
0.5	0	0.5	0
0	0	0	0

Figure 3 show the cfu of *E. coli* and *S. aureus* after being incubated overnight with different concentrations of ZnO-NPs. 2.5 mg/mL for *E. coli* and 1 mg/mL for *S.aureus* were the minimum concentration of ZnO-NPs required forgrowth inhibition of both bacteria. Similar result was found in a previous published study which reported that 3.4 and 1 mg/mlfor *E. coli* and *S. aureus*, respectively, were the required MIC of ZnO-NPs [5-17].

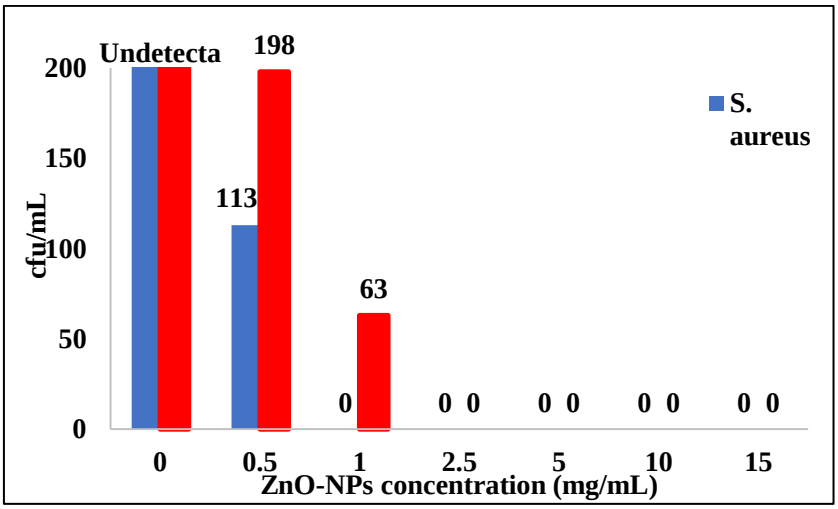

Figure 3.cfu of E. coli and S. aureus with different concentrations of ZnO-NPs

Tables 3 and 4 show a summary of MIC and MBC results for *E. coli* and *S. aureus*, respectively. It was found that higher concentration of ZnO-NPs is required for growth inhabitation for gram-negative bacteria as compare to that of gram-positive bacteria. This could be due to different reasons such as the wall structure of the cell, contact degree or physiology of the cell [18].

Table 3. Determination of MIC and MBC for E. coli.

Mode of effect	Concentration (mg/mL)
Growth	0.5
Growth	1
Bacteriostatic	2.5 (MIC)
Bacteriostatic	5
Bacteriostatic	10
Bactericidal	15 (MBC)

Table 4. Determination of MIC and MBC for S. aureus.

Mode of effect	Concentration (mg/mL)
Growth	0.5
Bacteriostatic	1(MIC)
Bacteriostatic	2.5
Bacteriostatic	5
Bacteriostatic	10
Bactericidal	15 (MBC)

Figures 4 and 5 show the cfu of both test bacteria with time as a factor. The time-dependent study of ZnO-NPs antibacterial activity showed that for all the concentrations, the cfu of the tested bacteria was decreased gradually during 72 h. Moreover, in all the concentrations of ZnO-NPs, it was found that cfu was undetectable after 7 h of the experiment.Based on the results, it can be suggested that ZnO-NPs are efficacious antibacterial agent on *E. coli* and *S. aureus* bacteria.

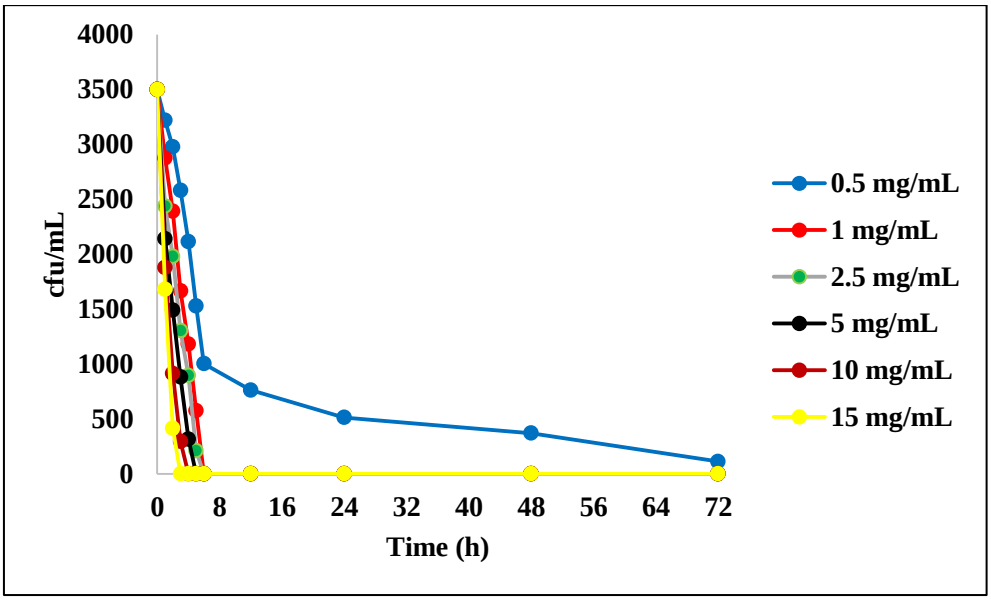

Figure 4. cfu of E. coliwith respect of time

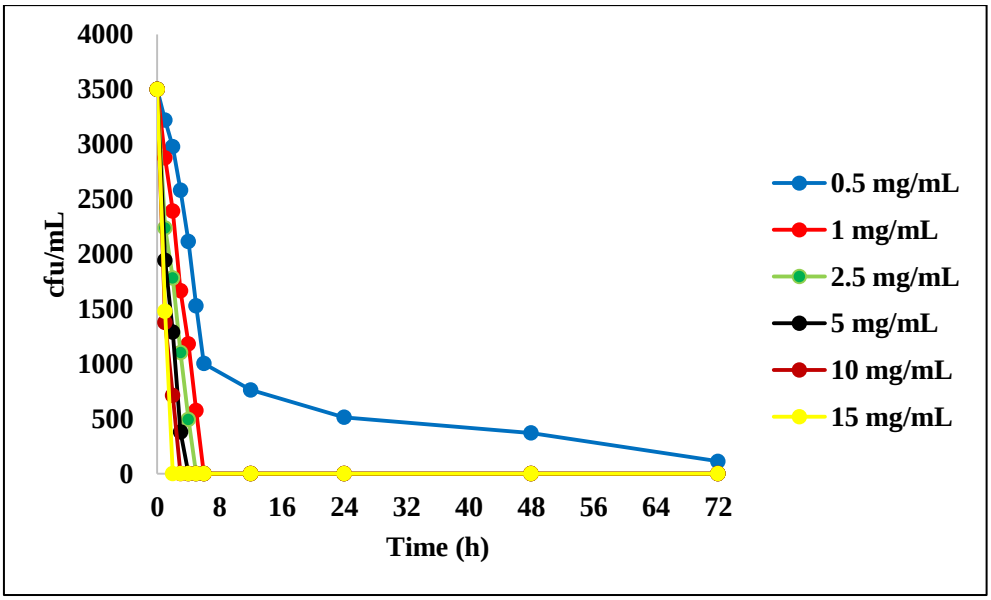

Figure 5. cfu of S. aureuswith respect of time

4. Conclusion

Chemical method was used to successfully synthesized zinc oxide nanoparticles with using Poly Vinyl Alcohol (PVA) as a surfactant.

The particles structure of the prepared ZnO-NPs was investigated by Transmission Electron Microscopy (TEM). TEM image revealed that the particle size of ZnO-NPs was at nano scale level. The synthesized ZnO-NPs was found to be an applicable potential alternative anticancer drug rather than the traditional other than the camptothecin drug. Different concentrations of ZnO-NPs were used in the cytotoxicity in vitro study and the results indicated that varying the concentrations of ZnO-NPs resulted in several phases of the cell death. The prepared ZnO-NPs showed necrosis of the MCF-7 cells at 100 mg/mL. Based on the results, it can be concluded that ZnO-NPs are effective antibacterial agent both on *E. coli* and *S. aureus* bacteria.

References

1- Matei, A., Cernica, I., Cadar, O., Roman, C., & Schiopu, V. (2008). Synthesis and characterization of ZnO – polymer nanocomposites. *Int. J. Mater. Form*. 1, 767-770.

2- Mohammed, M., Rozyanty,A. R., Adam,T., & Betar, B. O. (2017). ZnO characterization, UV and photocatalysis mechanism for water repellent phenomena in polymer poly composite. *AIP Conf. Proc*., 1885, 020215.

3- Priyanka, G., Brian, P., David, W. B., Wenjie, H., William, P. J., &Anne, J. A. (2009). Antimicrobial activities of commercial nanoparticles against an environmental soil microbe, Pseudomonas putida KT2440. *J. Bio. Eng*., 3, 1-13.

4- Mohammed, M., Rozyanty, R., Mohammed,A. M., Osman, A. F., Adam, T., Dahham, O. S., Hashim, U., Noriman, N. Z., &Betar, B. O. (2018). Effect of kenaf fibre Mat layers and Zinc Oxide Nanoparticle Concentration on the Mechanical and Thermal Properties of ZnONPs/kenaf/polyester Composites. *IOP Conf. Ser.: Mater. Sci. Eng*., 454, 012079.

5- Reddy, K. M., Kevin, F., Jason, B., Denise, G. W., Cory, H., &Alex, P. (2007). Selective toxicity of zinc oxide nanoparticles to prokaryotic and eukaryotic systems. *J. Appl. Phys. Lett*., 90. 1-3.

6- Mohammed, M., Rozyanty, A. R., Osman, A. F., Adam, T., Hashim, U., Mohammed,A. M., Noriman, N. Z., Dahham, O. S.,Betar, B. O. (2017). The Weathering Effect in Natural Environment on KenafBast Filled Unsaturated Polyester Composite and Integration of Nano Zinc particle for Water Repellent. *Micro and Nanosystems*, 9, 16-27.

7- Nagarajan, P., Rajagopalan, V. (2008). Enhanced bioactivity of ZnO nanoparticles-an antimicrobialstudy. *J. Sci. Technol. Adv. Mater.*, 9, 035004.

8- Mohammed, M., Rozyanty, A. R., Osman, Mohammed, A. M., Osman, A. F., Adam, T., Dahham, O. S.,Hashim, U., Noriman, N. Z., Betar, B. O. (2018). Fabrication and Characterization of Zinc Oxide Nanoparticle-treated Kenaf Polymer Composites for Weather Resistance Based on a Solar UV Radiation. BioResources, 13, 6480-6496.

9- Rizwan, W., Young-Soon, K., Amrita, M., Soon-Il, Y., & Hyung-Shik, S. (2010). Formation of ZnOmicro-flowers prepared via solution process and their antibacterial activity. *J. Nanoscale Res. Lett.*, 5, 1675–1681.

10- Mohammed, M., Betar, B. O.,Rozyanty, R., Mohammed, Osman, A. F., Jaafar, M., Adam, T., Dahham, O. S., Hashim, U., &Noriman, N. Z. (2019). Zinc Oxide Nano Particles Integrated Kenaf/Unsaturated Polyester BioComposite. *J. Renew. Mater.*, 7, 967-982.

11- Prashanth, G. K., Prashanth, P.A., Bora, U., Gadewar, M., Nagabhushana, B. M., Krishnaiah, A. G. M., Sathyananda, H. M. (2105). In vitro antibacterial and cytotoxicity studies of ZnO nanopowders prepared by combustion assisted facile green synthesis. *Int. J. Mod. Sci.*,1, 67-77.

12- Chandrasekhar, M., Nagabhushana, H., Sharma, S. C., Sudheerkumar, K. H., Dhananjaya, N., Sunitha, D. V., Shivakumara, C., & Nagabhushana, B. M. (2014). Particle size, morphology and color tunable ZnO:Eu^{3+}þnanophosphors via plant latex mediated green combustion synthesis. *J. Alloys Compd.*, 584, 417-424.

13- Hanley, C., Layne, J., Punnoose, A., Reddy, K. M., Coombs, I., Coombs, A., Feris, K., &Wingett, D.(2008). Preferential killing of

cancer cells and activated human T cells using ZnO nanoparticles.*Nanotechnology*, 19, 295103.
14- Dadashazadeh, S., Derakhashandeh, K., Erfan, M. (2007). Encapsulation of 9-nitrocamphothecin,aovel anticancer drug, in biodegradable nanoparticles: factorialdesign, characterization andrelease kinetics.*Eur. J. Pharm. Biopharm.*, 66, 34-41.
15- Serpe, L., Catalano, M., Cavalli, R., Ugazio, E., Basco, O., Canaparo, R., Munton, E.,Friaria, R., Grasco, M.R., Eandi, M., &Zara, G.P. (2009). Cytotoxicity of anticancer drugsincorporated in solid lipid nanoparticles on HT-29 colorectal cancer cell line. *Eur. J. Pharm. Biopharm.*, 58, 673-680.
16- Rizwan, W., Nagendra, K. K, Akhilesh, K. V, Anurag, M., Hwang, I. H, You-Bing, Y., Hyung Shik, S. h, Young-Soon, K. (2010). Fabrication and growthmechanism of ZnO nanostructures and their cytotoxic effect onhuman brain tumor U87, cervical cancer HeLa, and normal HEKcells. *J. Biol. Inorg. Chem*., 16, 431-442.
17- Salem, I. A. S., Rozyanty, A. R., Betar, B. O., Adam, T., Mohammed, M., & Mohammed, A. M. (2017). Study of the effect of surface treatment of kenaf fiber on chemical structure and water absorption of kenaf filled unsaturated polyester composite. J. Phys. Conf. Ser., 908, 012001.
18- Selahattin, A., Kadri, G., & Ramazan, C. (1998). The effect of zinc on microbialgrowth. *Tr. J. Med. Sci.*, 28, 595-597.

Pulmonary Aspergillosis-Associated COVID-19

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Abstract:

New health problems are emerging as the global COVID-19 pandemic spreads internationally. The need for effective COVID-19 testing methods, therapies and vaccinations is the biggest global emergency. Although these goals are especially important, the elevated risk of co-infection is not only a serious threat to health systems, but also a threat to the lives of patients. Pulmonary aspergillosis syndromes that complicate extreme viral infections are distinguished from classical invasive aspergillosis, which is most widely recognized in people with neutropenia and other immunocompromised individuals. This article highlights on a serious threat during the COVID-19 pandemic, aspergillus can cause co-infection with SARS-CoV-2 and the Challenges of CAPA.

Keywords: COVID-19, CAPA, Aspergillosis, viral infection.

Introduction:

Aspergillosis, combined with extreme viral infection, contains a constellation of airway-invasive and angio-invasive diseases and results in risks associated with poor clearance and killing of airway fungus, including epithelial damage associated with virus or inflammation, systemic immunosuppression, and underlying lung disease. Radiologic abnormalities may vary, reflecting different pathologies. The urgent need for strategies to improve diagnosis, treatment and prevention is illustrated by prospective studies reporting poor results in patients with CAPA (Covid-19 Associated Pulmonary Aspergillosis). Invasive aspergillosis is commonly recognized in individuals with severe

immunosuppression, especially those associated with transplantation and hematologic malignancies. It is characterized by hyphal invasion, with possible vascular invasion and hallmark radiographic findings reflecting hemorrhage and necrosis by bronchial or lower airway tissues [1,2]. In spite of decades of case reporting, many clinicians still fail to realize, that in individuals with severe influenza, Aspergillus species may cause destructive inflammatory and invasive pathology, wrongly ascribing culture findings to benign colonization of the airway. pathophysiology of CAPA is different and not inherently related to invasive aspergillosis that occurs in classically immunosuppressed individuals. Specific pathophysiology of these syndromes involves poor clearance of conidia, causing bronchial inflammation and invasion, manifesting with separate radiographic and clinical findings characteristic of airway invasion with slower development of necrosis, and exuberant and chronic tracheobronchiti s, sometimes with lack of angioinvasion, restricting serum-based diagnostic performance. Figure (1). [3,4,5].

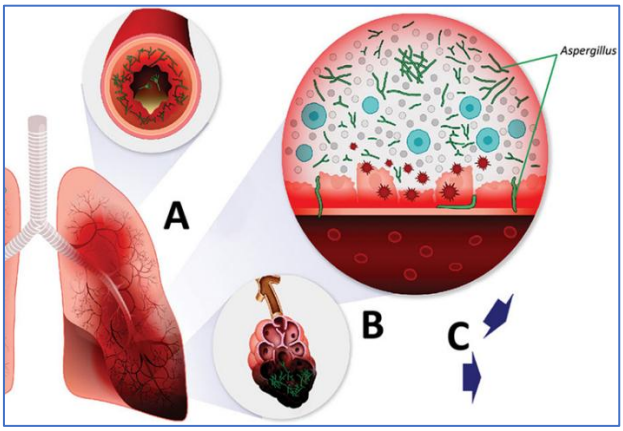

Figure 1. coronavirus disease–associated pulmonary aspergillosis. a: tracheobronchitis and obstructive pneumonia and complications (nodules, cavity necrosis, pleural invasion) of invasive fungal pneumonia, b: pathologic airway inflammation and excess mucous development is caused by aspergillus overgrowth., c: of alveoli. invasive pneumonia is caused by hyphal growth. post-obstructive bacterial pneumonia from invasive aspergillosis tracheobronchitis

Evidence indicate that Aspergillus airway overgrowth with pulmonary infection, similarly distinguish by mixed airway inflammation and bronchial invasion, may cause serious respiratory virus infections, especially influenza and infection with severe acute respiratory syndrome coronavirus 2. Distinction between the colonization of benign airways and emerging diseases caused by *Aspergillus Spp.* Conidia are normal inhabitants of the airways and do not often cause inflammatory or invasive diseases, which has always been difficult. [6, 7, 8]. When one assumes that CAPA may be a constellation of mixed airways and invasive diseases, radiographic manifestations can be better known. [9,10] The most common species causing co-infection in patients with COVID-19 was *A. fumigatus*, followed by *A. flavus* [11, 12]. Voriconazole is the most widely used antifungal agent and the recommended anti-Aspergillus agent, aspergillosis caused by azole-resistant Aspergillus is also possible. [13, 14, 15]. And can the potential for drug-drug interactions with nti-SARS-CoV-2 agents [16]. The efficacy of the use of Voriconazole in COVID-19 patients receiving anti-SARS-CoV-2 agents should therefore be investigated in further studies. In addition, a new anti-mold azole vuconazole, which does not have the side effect, may require more research on its potential role in the treatment of Invasive Pulmonary Aspergillosis - COVID-19[17] Though many questions stay, emerging confirmation supports the outcome that in COVID-19 patients, Aspergillus species cause serious pathology, ranging from inflammation of the airway to semi-acute or acute bronchial invasion, close, for the most part, to that seen with serious influenza infections. Increased effort is required to identify the best ways to prevent, diagnose and treat COVID-19-related Aspergillus disease.

References:

[1] Kosmidis, C. and Denning, D.W., 2015. The clinical spectrum of pulmonary aspergillosis. Thorax, 70(3), pp.270-277.

[2] Marr, K.A., Platt, A., Tornheim, J.A., Zhang, S.X., Datta, K., Cardozo, C. and Garcia-Vidal, C., 2020. Aspergillosis Complicating Severe Coronavirus Disease. Emerging Infectious Diseases, 27(1).

[3] Bartoletti, M., Pascale, R., Cricca, M., Rinaldi, M., Maccaro, A., Bussini, L., Fornaro, G., Tonetti, T., Pizzilli, G., Francalanci, E. and Giuntoli, L., 2020. Epidemiology of invasive pulmonary aspergillosis among COVID-19 intubated patients: a prospective study. Clinical Infectious Diseases.

[4] Falces- Romero, I., Ruiz- Bastián, M., Díaz- Pollán, B., Maseda, E., García- Rodríguez, J. and SARS- CoV- 2 Working Group, 2020. Isolation of Aspergillus spp. in respiratory samples of patients with COVID- 19 in a Spanish tertiary care hospital. Mycoses, 63(11), pp.1144-1148.

[5] Van Arkel, A.L., Rijpstra, T. A., Belderbos, H. N., Van Wijngaarden, P., Verweij, P. E. and Bentvelsen, R.G., 2020. COVID-19- associated pulmonary aspergillosis. American journal of respiratory and critical care medicine, 202(1), pp.132-135.

[6] Blot, S. I., Taccone, F.S., Van den Abeele, A.M., Bulpa, P., Meersseman, W., Brusselaers, N., Dimopoulos, G., Paiva, J. A., Misset, B., Rello, J. and Vandewoude, K., 2012. A clinical algorithm to diagnose invasive pulmonary aspergillosis in critically ill patients. American journal of respiratory and critical care medicine, 186(1), pp.56-64.

[7] Bassetti, M., Giacobbe, D. R., Grecchi, C., Rebuffi, C., Zuccaro, V. and Scudeller, L., 2020. FUNDICU investigators. Performance of existing definitions and tests for the diagnosis of invasive aspergillosis in critically ill, adult patients: a systematic review with qualitative evidence synthesis. J Infect, 81, pp.131-146.

[8] White, L., Dhillon, R., Cordey, A., Hughes, H., Faggian, F., Soni, S., Pandey, M., Whitaker, H., May, A., Morgan, M. and Wise, M., 2020. A national strategy to diagnose COVID-19 associated invasive fungal disease in the ICU.

[9] Rutsaert, L., Steinfort, N., Van Hunsel, T., Bomans, P., Naesens, R., Mertes, H., Dits, H. and Van Regenmortel, N., 2020. COVID-19-

associated invasive pulmonary aspergillosis. Annals of Intensive Care, 10(1), pp.1-4.
[10] Falces Romero, I., Ruiz Bastián, M., Díaz Pollán, B., Maseda, E., García Rodríguez, J. and SARS- CoV- 2 Working Group, 2020. Isolation of Aspergillus spp. in respiratory samples of patients with COVID- 19 in a Spanish tertiary care hospital. Mycoses, 63(11), pp.1144-1148.
[11] Chen, F. L., Wang, C. H., Hung, C. S., Su, Y. S. and Lee, W.S., 2020. Co-infection with an atypical pathogen of COVID-19 in a young. Journal of Microbiology, Immunology, and Infection.
[12] Rawson, T.M., Moore, L.S., Zhu, N., Ranganathan, N., Skolimowska, K., Gilchrist, M., Satta, G., Cooke, G. and Holmes, A., 2020. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clinical Infectious Diseases.
[13] El-Baba, F., Gao, Y. and Soubani, A.O., 2020. Pulmonary Aspergillosis: What the Generalist Needs to Know. The American Journal of Medicine.
[14] Antinori, S., Rech, R., Galimberti, L., Castelli, A., Angeli, E., Fossali, T., Bernasconi, D., Covizzi, A., Bonazzetti, C., Torre, A. and Carsana, L., 2020. Invasive pulmonary aspergillosis complicating SARS-CoV-2 pneumonia: A diagnostic challenge. Travel Medicine and Infectious Disease.
[15] Meijer, E.F., Dofferhoff, A.S., Hoiting, O., Buil, J.B. and Meis, J.F., 2020. Azole-Resistant COVID-19-Associated Pulmonary Aspergillosis in an Immunocompetent Host: A Case Report. Journal of Fungi, 6(2), p.79.
[16] Varshneya, M., Irurzun-Arana, I., Campana, C., Dariolli, R., Gutierrez, A., Pullinger, T.K. and Sobie, E.A., 2020. Investigational treatments for COVID-19 may increase ventricular arrhythmia risk through drug interactions. medRxiv.
[17] Prattes, J., Valentin, T., Hoenigl, M., Talakic, E., Reisinger, A. C. and Eller, P., 2020. Invasive pulmonary aspergillosis complicating COVID-19 in the ICU-A case report. Medical Mycology Case Reports.

Food and Nutrition Safety During the COVID-19 pandemic period

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Abstract:

The world still faces an unprecedented threat from the COVID-19 pandemic caused by the SARS-COV. Many Arab and international countries have followed the advice of the world health organization regarding the introduction of social distancing as one of the ways to reduce the transmission of the virus, as well as closing restaurants and markets selling fruits, vegetables, canned foods, meat and animals. There is currently no evidence that people can develop COVID-19 after eating a certain type of food, including fruits and vegetables. Although fresh fruits and vegetables are part of a healthy diet that doctors encourage eating, it may be a vector for some microorganisms such as viruses. However, workers in the food industry do not have the opportunity to work from home and are required to continue working in their usual place of work. As the preservation of all workers in healthy and safe food production and supply chains is critical to surviving the current epidemic, and this is required to maintain the safety of workers and consumers, with confidence between workers and consumers in terms of food availability and safety from viruses [1, 2].

Food Safety Management

Food industry laboratories and restaurants should have Food Safety Management System- FSMS based on Hazard Analysis Critical Control Point- HACCP in place for food safety management and food contamination prevention. FSMS food safety management systems are supported by prerequisite programs that include good hygiene

practices, proper cleaning and sanitation, zoning of processing areas, supplier control, warehousing, distribution and transportation, employee hygiene and fitness at work, and all basic conditions and activities necessary to maintain a healthy food environment. Some sources emphasized that it is very unlikely that people will contract COVID-19 while packaging food or foodstuffs themselves, on the grounds that it is a respiratory disease and the main transmission route is through direct contact between people and through droplets that are generated when a person with the virus coughs or sneezes. Coronaviruses cannot reproduce in food. As the new Corona virus needs an animal or a human host to reproduce, and the World Health Organization confirms this, and the virus can also spread indirectly by touching contaminated objects such as elevator buttons and doors. Where heavy respiratory droplets fall so that they cannot be carried in the air, so things and surfaces surrounding the infected person land on them, and it is possible for a person to be infected by touching a contaminated surface, object, or an infected hand (with a handshake, for example) and then touching his mouth, nose, or eyes [3, 4].

Recent research has evaluated the survival of the emerging corona virus on different surfaces and reported that the virus can survive for up to 72 hours on plastic and stainless steel, up to four hours on copper, and up to 24 hours on cardboard, paper and banknotes. This research was conducted under laboratory conditions (control of relative humidity and temperature). Therefore, it is necessary for laboratories and restaurants in the food industry and preparation to enhance hygiene measures and provide periodic training on food hygiene principles to eliminate or reduce the risks of contaminated food by using personal protective equipment (PPE), such as masks, gloves and a special coat to be effective in limiting the spread of viruses and diseases. In addition, commitment to staying at social distances between employers and workers, how to sterilize toilets, bathrooms and sanitation, and to

promote frequent and effective hand washing at every stage of food processing, processing and marketing [5, 6].

These measures will protect employees from the spread of COVID-19 among workers, maintain a healthy workforce, and detect and exclude infected food handlers and direct contacts from the workplace. Although the virus's genetic material (RNA) was isolated from the stool samples of infected patients, there is no confirmed research, reports, or any evidence of fecal-oral transmission. In some cases, people infected with the virus may have no symptoms, that is, they do not show any signs or symptoms of the disease, or they may be present with mild symptoms that can be easily overlooked. Some infected people who have not yet developed symptoms may be able to spread the virus. This emphasizes the need for all individuals working in the food industry, regardless of their apparent health condition, to practice personal hygiene and use personal protective equipment appropriately with periodic virus testing, and to allow employees to report disease by phone or email, this must be proven with reports medical. Good employee health practices can be summarized as follows [7, 8]:

- **Hand hygiene:** washing with soap and water for at least 20 seconds (follow the advice of the World Health Organization) with frequent use of hand sanitizers and hand sanitizers that contain ethyl alcohol (70 - 75%).
- Covering the mouth and nose when coughing or sneezing.
- Frequent cleaning and disinfection of work surfaces and touch points such as door handles.
- Avoid close contact with anyone showing symptoms of respiratory illnesses such as coughing, sneezing, cold and fever.
- Gloves can be used by food workers, but they must be changed frequently and hands must be washed between changing gloves and when gloves are removed. Workers should avoid touching their mouths

and eyes when wearing gloves. Disposable gloves should not be used for food work as an alternative to washing hands. Wearing disposable gloves can give a false sense of security and may lead to employees not having to wash hands as frequently as needed.

- Physical distancing is very important to help slow the spread of the virus. Steer distance as far as reasonably possible. Maintain a distance of at least 1 meter (3 feet) between co-workers. Where the food production environment makes it difficult to do so.
- Provide clean hair clips and coats, and reduce slipping by wearing suitable work shoes for employees.
- The driver must be equipped with hand sanitizers, hand sanitizers and paper towels.
- Clean and sterilized containers and packaging should be used.
- The driver conducting the food delivery must be aware of the potential risks involved in the transmission of the virus by contact. The virus can be caught if drivers come into contact with contaminated surfaces, the hands of an infected person, wheels, door handles, mobile devices, etc.
- Regulating the number of visitors entering a retail store to avoid overcrowding; And placing signs at entry points asking visitors not to do so to enter the store if they are unwell or show symptoms of COVID19. Hand sanitizers, spray disinfectants, and disposable paper towels should be provided at store entry points, use of floor markers within the retail store and facilitate compliance with physical distance, especially in more crowded areas, such as meter service.
- Encouraging the use of contactless payments.
- Keep doors open where possible to reduce contact.

How Can You Protect Yourself?

The virus that causes COVID-19 has not been found in drinking water. The Environmental Protection Agency regulates water treatment

plants to ensure that the treated water is safe to drink. Pathogenic bacteria grow faster between 37 - 40 ° C in meat, poultry or seafood, so it is best to keep them refrigerated or during transportation. In the event of a leakage from the food container, a secondary container or boxes for meat and meat products must be brought and placed in the car so that it can be easily cleaned and sterilized. To clean surfaces, it is preferred to follow the following methods [9, 10]:

• Clean countertops, benches, faucets, light switches, door handles, etc. with LIQUID LAUNDRY DETERGENT (disinfectant solution) DIY containing Borax or add 5 tablespoons (1/3 cup) of unscented liquid chlorine bleach (sodium hypochlorite) to 1 liter of water. Be careful not to mix the solution with shampoo or other detergents to prevent the release of toxic methane gas from it.

• The use of ethanol alcohol at a concentration of 70 - 75%.

At present, there is no evidence that you can contract the virus that causes COVID-19 by eating wild game. However, hunters can contract other diseases when handling or eating animal skins and blood undercooked. Hunters should always practice good hygiene when handling animals by following the following food safety recommendations [11, 12]:

• Not to mix seafood with poultry and other meat.

• Not to hunt animals that appears sick or dead.

• Maintaining the cleanliness of the meat during storage and cooling it as soon as possible after hunting the animal.

• Avoid cutting the spine and spinal tissues, while beware of eating the brains of any wild animal.

• Wear rubber gloves or disposable gloves.

• Wash hands carefully with soap and water, and it is preferable to use disinfectants and sterilizers as well.

• Knives, equipment, and surfaces that have been in contact with game of game should be cleaned with soap and water and sterilized with an appropriate sterilizer.
• Cook all game meat thoroughly (up to an internal temperature of 165°F or higher).
• You should not eat raw wild meat or uncooked dishes that contain wild animal blood, because such practices put people at risk of contracting many types of infections.

Vitamins C and D, in addition to zinc may have positive effects on how the immune system works and fight infections. the best way to obtain these nutrients is through foods: vitamin C in fruits and vegetables; vitamin D in low-fat milk and fortified milk substitutes; and zinc in seafood, lean meats, legumes, nuts and seeds, in some cases, nutritional supplements may have unwanted effects, especially if they are eaten in very large quantities, or if the person has certain health conditions. advice on purchasing prepackaged and prepackaged goods is provided on the feeding boxes. getting the right amount of nutritious foods like lots of fruits and vegetables, lean protein, and whole grains is important for health [13, 14].

Anti-virus Foods to Build Immunity and Ward off Disease

• **Garlic:** It is a powerful anti-virus. It can be eaten raw, mashed, or added to soups.
• **Star anise:** The spices in the form of a flower contain Shikimic acid, which is used as a basic material for the production of Tamiflu, which is used for the influenza virus. It is very powerful as an anti-virus. Star anise is taken by placing it in boiling water, with or without green tea or black tea (Figure 1).
• **Ginger:** Ground ginger is taken with star anise and a little honey and lemon (Figure 2).

• **Coconut oil**: You can cook your food with coconut oil, as lauric acid or dodecanoic acid - $C_{12}H_{24}O_2$, as the oil contains caprylic acid (Caprylic Acid (Octanoic Acid), which are necessary to strengthen the immune system against viruses (Figure 3).

Figure 1: Star anise

Figure 2: Ginger, lemon and anise as a drink to treat respiratory and viral diseases

Figure 3: Coconut Oil

• **Foods rich in Resveratrol:** such as peanuts, pistachios, grapes, red and white wine, cranberries, strawberries, cocoa, and dark chocolate help in fighting fungal and viral infections and stress (Figure 4).

Figure 4: Some Foods Rich in Resveratrol

• **Foods rich in vitamin C:** such as oranges, lemons, red peppers, yellow peppers, pineapples, papaya, strawberries, broccoli, cauliflower, tomatoes, kiwis, and vitamin C supplements are necessary to raise the body's immunity against bacterial and viral infections.

In the case of viral respiratory diseases, it is advised to eat a lot of warm vegetable soup, dried thyme, olive oil, fish oil, turmeric and ginger, which boosts the immune system. The Chinese also used essential oils such as thyme, eucalyptus, or anise oil [15, 16].

References:

1. Critical preparedness, readiness and response actions for COVID-19: Interim guidance 19 March 2020 https://www.who.int/publicationsdetail/critical-preparedness-readiness-and-responseactions-for-covid-19

2. Codex Alimentarius. Food hygiene: Basic texts http://www.fao.org/3/a1552e /a1552e00.pdf

3. Coronavirus disease 2019 (COVID-19) Situation Report – 66 https://www.who.int/docs/defaultsource/coronaviruse/situation-reports/20200326- sitrep-66-covid-19.pdf? sfvrsn=81b94e61_2

4. Liu J, Liao X, Qian S *et al*. Community transmission of severe acute respiratory syndrome coronavirus 2, Shenzhen, China, 2020. Emerg Infect Dis 2020 doi.org/10.3201/eid2606.200239

5. Chan J, Yuan S, Kok K *et al*. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020 doi: 10.1016/S0140-6736(20)30154-9

6. Li Q, Guan X, Wu P, *et al*. Early transmission dynamics in Wuhan, China, of novel coronavirusinfected pneumonia. N Engl J Med 2020; doi:10.1056/NEJMoa2001316.

7. Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497–506.

8. Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, *et al*. Active monitoring of persons exposed to patients with confirmed COVID-19 - United States, January–February 2020. MMWR Morb Mortal Wkly Rep. 2020 doi: 10. 15585/mmwr.mm6909e1external icon

9. World Health Organization. Report of the WHO China Joint Mission on Coronavirus Disease 2019 (COVID-19) 16-24 February 2020 [Internet]. Geneva: World Health Organization; 2020 Available from:

https://www.who.int/docs/defaultsource/ coronaviruse/who-china-joint-mission-oncovid-19-final-report.pdf

10. Ong SW, Tan YK, Chia PY, Lee TH, Ng OT, Wong MS, *et al*. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA. 2020 Mar 4 [Epub ahead of print].

11. van Doremalen N, Bushmaker T, Morris DH et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020 Mar 17. doi: 10.1056/NEJMc2004973

12. Coronavirus disease (COVID-19) advice for the public. https://www.who.int/ emergencies/diseases/novelcoronavirus-2019/advice-for-public

13. Q&A on coronaviruses (COVID-19) https://www.who.int/news-room/q-a-detail/q-acoronaviruses

14. Yu P, Zhu J, Zhang Z, Han Y. A familial cluster of infection associated with the 2019 novel coronavirus indicating possible person-to-person transmission during the incubation period. J Infect 2020, doi: 10.1093/jiaa077.

15.https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/food-and-COVID-19.html#:~:text=Currently%2C%20there%20is%20no%20evidence,coughs%2C%20sneezes%2C%20or%20talks., Food and Coronavirus Disease 2019 (COVID-19), Aug. 22, 2020.

16.https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/food-and-nutrition-tips-during-self-quarantine, 2020.

Health Study Into the Effect of COVID-19 on the Sense of Smell and Taste Among Infected People

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Abstract

Loss of smell has emerged as one of the most common symptoms of COVID-19 infection, with anecdotal reports from Europe, Asia, the United States and the rest of the world quickly giving way to the CDC adding a new loss of smell and taste to its list of symptoms in examining the virus. It was found that among the most common neurological symptoms caused by the Corona virus is the loss of the sense of smell and taste, which may be the first evidence that a person has contracted Covid-19. Coronaviruses are known for their ability to infect the respiratory system and damage it to varying degrees, some Coronaviruses are similar in effect to regular influenza, and some of them destroy lung cells and have claimed thousands of lives so far. Viruses are constantly evolving in an attempt to triumph over the immune system and dominate the patient's body. In this research, we study the effect of the coronavirus, known as Corona virus, on a person's respiratory system and natural remedies for it.

Introduction:

Corona virus was first discovered in China in December 2019 and the World Health Organization officially declared it a global pandemic on March 11, 2020. At that point, there were more than 118,000 cases in 114 countries, and 4,291 people lost their lives, according to a briefing from WHO Director-General Tedros Adhanom Ghebreysos.

As of June 2, 2020, 6,194,533 cases worldwide and 376,320 deaths have been confirmed and numbers are still increasing until the time of preparing this paper [1, 2]. According to the National Institute of Allergy and Infectious Diseases (NIAID) [3]. One strain of the virus family (SARS-CoV-2) causes COVID-19 the disease responsible for the global epidemic that generally leads to mild or moderate respiratory illnesses and increases in severity and severity depending on the patient's immunity. Among the most common neurological symptoms it causes are headache, dizziness, loss of consciousness, weakness, seizures, paralysis, strokes and more. The virus spreads through particles in the air, so it enters the body first through the nose and mouth, and when this happens, it is likely that the virus will then cross the bone in the upper part of the nose, to reach the olfactory bulb that includes the olfactory nerve and its branches. If the virus damages these nerves, a person may lose their sense of smell, while if the virus invades the taste buds directly, it can prevent nerve fibers from sending signals to the brain and cause a person to lose a sense of taste. Temporary loss of smell when you have a virus is normal, but sometimes this symptom can continue even after the rest of the body has get well [4, 5]. It is still too early to determine how likely the CORONA virus may cause long-term odor problems. However, if you or anyone you know get well from the disease but are still struggling to pick up a scent from your favorite scent, this is something you should take seriously. For most COVID-19 patients with olfactory loss, the sensation returns within a few weeks, and doctors do not yet know whether the virus causes long-term odor loss, while the inability to smell may appear to be a small side effect, the results can be devastating (figure 1) [6].

Figure 1: entering the virus via aerosols into respiratory tract

The sensation is intricately associated with self-preservation - the ability to smell fire, chemical leaks, or rotten food - and our ability to capture complex tastes and enjoy food .According to the German medical site, "Pharmazeutische Zeitung" About 85% of people with Cofed19 say that, among other symptoms, they suffer from olfactory disorders, which can range from a severe deficiency to a complete loss of sense of smell, which may last several days [7].

The international team of researchers surveyed 187 Italians who were infected with the virus but were not sick enough to be hospitalized. Individuals were asked to assess their sense of smell or taste shortly after diagnosis and again a month later. A total of 113 reported a change in their sense of smell and/ or taste: 55 said they had fully get well. And 46 reported an improvement in their symptoms. 2 They found that their symptoms were not changed or worse, and it was found through the study that people who had severe symptoms took longer to improve. Professor Claire Hopkins [8], one of the researchers and president of the British Association of Rhinology, confirmed that her team is now conducting more research on people who suffer from long-term symptoms. She told the BBC: “The data from other viral

diseases, and some new data that we are collecting, indicate that the vast majority of people will get better, but for some, the get well will be slow". For people who get well more quickly, it is likely the virus. It may only affect the cells lining their nose. For people get well more slowly, the virus may have affected the nerves involved in scent as well. These neurons could take longer to repair and regenerate.

The mechanism of working the sense of smell system

The olfactory system, which allows humans and other animals to smell, is basically a way to decrypt chemical information. When someone inhales a large tattoo, the molecules move to the top of the nose to the olfactory epithelium, a small piece of tissue at the back of the nasal cavity. These molecules are connected to olfactory sensory neurons, which then send a signal through acolyx, a long tail that passes through the skull and delivers this message to the brain, which records molecules such as coffee, skin or rotting lettuce [9] .Scientists still don't fully understand this system, including exactly what happens when it stops working. Most people don't realize how common odor loss really is, says Stephen Munger, director of the Center for Smell and Taste at the University of Florida, told CNN. "This lack of general understanding means that there is less interest in trying to understand the basic functions of the system" [10]. People can lose their sense of smell after a viral infection, such as influenza or colds, or after a traumatic brain injury. Some are born with no sense of smell at all or lost due to cancer treatments or diseases such as Parkinson's disease and Alzheimer's disease. It may also fade with age. While olfactory disorders are not as obvious as hearing loss or visual impairment, data from the National Institutes of Health (NIH) [11] show that nearly 25 percent of Americans over the age of 40 report some kind of change in their sense of smell and more. 13 million people suffer from a measurable disorder such as loss of smell, loss of sense of smell, or

lack of sense of smell, which is a partial loss. Such conditions can last for years or even permanent. It is not clear whether the loss of sense of smell in COVID-19 is different from other cases of olfactory loss caused by a virus, but those with loss of smell due to COVID-19 appear to be unique in a few ways. First, they noticed the loss of sensation immediately because it is not accompanied by congestion or blockage that generally characterizes the early stages of virus-induced sense of smell loss. The other notable difference is that many patients with COVID-19 who reported loss of sense of smell get well relatively quickly, within a few weeks, unlike most people with olfactory loss from other viruses, which can last for months or years.

How can COVID-19 Affect the Ability to Smell?

Understanding which parts of the sense of smell system has been affected is a major first step towards discovering how the virus disrupts our ability to sense odors. When you have a cold, smell and taste is often difficult because your nose is stuffed and the airways are blocked. One study found that short-term loss of sense of smell may be caused by 'fissure syndrome [12], a condition in which soft tissues and mucus prevent odors from reaching olfactory neurons. But with Coved-19, the symptoms seem to stem from the way the disease invades the brain and nervous system because the virus does not tend to cause nasal obstruction, as researchers believe other research has also shown that the coronavirus can have serious neurological consequences beyond the olfactory system as in the form figure 2.

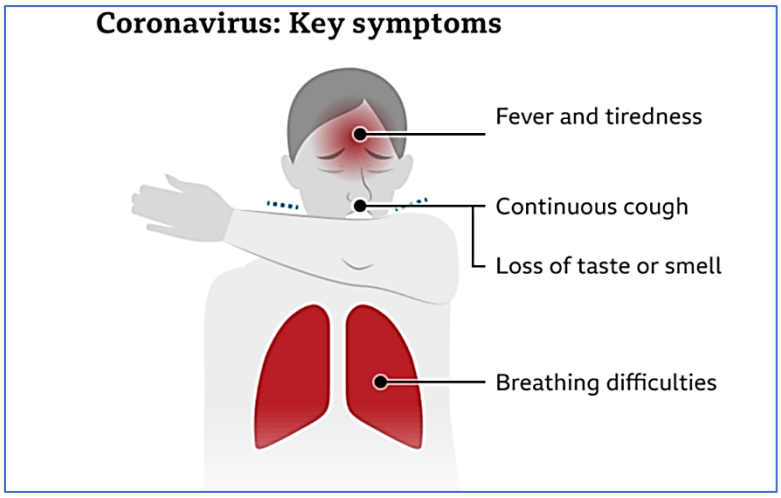

Figure 2: COVID 19 symptoms

The nose is one of the main places where SARS-CoV-2, causing COVID-19, enters the body. Researchers have already identified two types of nasal cells - cupal cells and ciliary cells - that are likely to be entry points for the virus .To understand how COVID-19 disrupts the sense of smell system, scientists first [13] [14] narrowed the list of potential targets of infection. SARS-CoV-2 needs a combination of protein (S TMPRSS2, ace2 enzyme to enter the cell. Protein S, which forms the spinal protrusions on the surface of the virus, is associated with the future of ACE2 on the surface of human cells, in a preliminary step for the virus to enter the cell. In addition to the lungs, this enzyme is found in other organs such as the small intestine, kidneys, heart, thyroid and testicle, so Data and other researchers have looked for weak cells in the olfactory system that expresses these proteins. They discovered that olfactory neurons, where the molecules bind and trigger a signaling mechanism to the brain, are not susceptible to COVID-19. Instead, in a paper published in Science Advances, Datta and colleagues showed that proteins appear in olfactory support cells, such as stem cells that regenerate neurons after exposure to damage, and in what are known as support cells. It helps support neurons physically, remove dead cells, and move odors through the mucus in the system.

In the nose and mouth, the virus is believed to be associated with ACE2 receptors in sensory neurons, and prevents these cells from facilitating the process of smelling and tasting as scientists have found a high level of ACE2 in Covid 19 patients. The action of this enzyme is determined by the conversion of angiotensin 1 to angiotensin 2, whose function is to increase sodium absorption in the kidney nephron, which in turn raises arterial blood pressure as well as stimulate heart contraction, vascular wall growth and the secretion of aldosterone, which increases sodium retention. If angiotensin 2 levels accumulate, blood vessels shrink and reduce blood flow to the organs, which may lead to damage. "These findings suggest that this area of the nose could be the point at which the virus enters the body", said Mingvi Chen, a research associate at Johns Hopkins University School of Medicine 'These results suggest that this area of the nose could be the point at which the virus enters the body [15]. Olfactory neurons work by moving charged ions across their membranes. If COVID-19 alters the concentration of ions surrounding these cells, it could make it impossible for neurons to send signals to the brain. The immune response could also disable the system in some way, or the inflammation could affect the part of the brain that processes odor.

Daniel Borsetto, MD, of Jay and St Thomas Hospitals in London [16], reported that only 12% of COVID-19 patients with mild symptoms reported a continuous loss of smell and taste after a month, while the rest had recently reported the same group. It made up of 202 patients with mild symptoms, isolated at home, and 64% reported a loss of taste or smell. The researchers said this study was conducted to report on the progression of these patients. All 202 patients were contacted 4 weeks after they tested positive for COVID-19 via reverse transcriptional polymerase chain reaction (PCR), and were interviewed about their symptoms. Symptom identification tools included the acute respiratory infection questionnaire and the outcome test on the sense of

smell and taste. Patients were also asked to rate their impairment on a six-point Likert scale. The 202 original patients, two died and 13 did not respond or refused a follow-up interview, so 187 patients were represented in the most recent survey. More than half of them were women and the average age was 56. Interestingly, 60.4% reported impaired sense of smell or taste in the two weeks prior to the test. The researchers also noted that of the 74 patients who did not report a change in smell or taste at baseline, 11 reported the onset of these symptoms, resulting in an increased "prevalence of smell or taste" to 66.3%. Overall, 55 patients reported a complete cure for odor or taste, 46 patients reported a decrease in severity, and 12 patients reported symptoms unchanged or worse. The 55 patients who had regained their sense of smell and taste, the mean duration of smell and taste was 11.2 days. The researchers said the limitations of the data include its self-reported nature, as well as the small sample size and that the study excluded patients who were severely ill. Interestingly, the SARS-CoV-2 swab test was repeated during the fourth week in 163 patients, still 52 patients.

Training People How to Smell Essential Oils

Because the olfactory nerve is unique in the way it travels directly through the memory center in the brain, aromatherapy has a special way of evoking memory. When you smell oils from a variety of families - floral, fruity, aromatic, and resinous - you are triggering multiple aspects of the scent to return.

Training people in the sense of smell with essential oils

Because the olfactory nerve is unique in the way it travels directly through the memory center in the brain, aromatherapy has a special way of evoking memory. When you smell oils from a variety of families - floral, fruity, aromatic, and resinous - you are triggering multiple aspects of the scent to return (figure 3).

Figure 3: Training people in the sense of smell with essential oils

Smell plays a role in our passion life, connecting us to our loved ones and memories. People who don't smell often report feeling isolated and depressed. Scientists are now beginning to reveal how COVID-19 affects this critical sense, hoping that these discoveries will help thousands of people with sense of smell. There is no research indicating that essential oils could also be helpful in diagnosing COVID-19. However, researchers at Hopkins University say it stands to reason that if the scent of essential oil - or any other scent you are familiar with - begins to smell, that indicates that something is happening with your scent. This doesn't necessarily mean it's COVID-19, but it will be an indication that you have to investigate further [17]. As people continue to get well from COVID-19, this interesting relationship between viruses and loss of smell and memory will become even more important. If you've get well from the vireos but are still having trouble smelling things around you or find that the familiar smell suddenly smells different, consider visiting your doctor to inquire about loss of sense of smell after the virus (and store some essential oils). One possibility may be smell training, or so-called smell training, a type of

nose physiotherapy that helps increase the efficiency of amplifying nerve signals. Every day, practitioners take a nice little inhaler from bottles of essential oils such as eucalyptus, cloves or lemons. When they smell, they focus on the smell, although they may not actually be able to smell it [19].

Artificial Intelligence Predicts Corona Infection

A British-American team [20] was able to develop a mobile application and a mathematical model that could predict with nearly 80% accuracy if a person is likely to be infected with "Covid-19" or not based on his symptoms and draws the artificial intelligence model - which the scientists developed in cooperation with the Health Sciences (ZOE) - its data from a free smartphone app called (COVID Symptom Study) launched by researchers in Britain on March 24, 2020, and in the United States on March 29, 2020, to collect data from individuals who report having any symptoms they have, and write down Their health with disease daily, and this includes symptoms, signs of hospitalization and data related to their medical history, as well as results of the classic reverse transcription polymerase chain reaction (RT-PCR) test. Tim Spector, leader of the research team at King's College London [17], said: The results of our study came as a surprise to us; Non-classic symptoms can be a strong indicator of infection, stressing that many governments do not take these factors into account, although they can help identify people with "Covid-19".

He explained: "Our results revealed that the loss of the senses of taste and smell is a major early warning sign of infection, and it should be included in the routine examination for the disease. He added "I advise anyone suffering from a sudden loss in these two senses to assume that he has Corona infection, and he should follow the self-isolation instructions in The house, until his infection is confirmed or not, to not spread the infection. "Also added that the team has also

developed a mathematical model that can predict with nearly 80% accuracy whether a person is likely to be infected with "Covid-19", based on his age, gender, and a combination of other major symptoms: loss of smell or taste, or severe coughing. Or constant fatigue and skipping meals [20].

Regarding the advantage of the new application, he indicated that the implications for it are of great benefit; Because in the absence of widespread and reliable testing for the Coronavirus, recording symptoms through the app is a simple, fast and cost-effective way to help people know whether or not they are infected, and the consequent steps to self-isolate and do the traditional test. Who can confirm or deny the injury [15].

Symptom Recording

During the study, which was conducted between March 24 and April 21, 2020, two million 450,569 people in Britain and 168,293 in America, between the ages of 16 and 90, reported their health condition through the application, which was downloaded by more than 3.5 million people in Britain and America. Just 6 weeks after its launch. About 800 thousand of the participants recorded symptoms related to "Covid-19", the most prominent of which was a feeling of fatigue and constant coughing with loss of appetite, in addition to losing the sense of smell and taste, then 18 thousand and 374 of them reported that they had taken a test to detect the Corona virus, and the test result was positive. It has 7 thousand and 178 of them, but the study researchers believe that the number of infected people based on the reported symptoms may reach 140 thousand of the total number of participants. The task of the team was to investigate the most prominent symptoms of the Corona virus, which were associated with positive cases, and the surprise was that they found that fever and cough (which is one of the most well-known symptoms of infection with the virus) were not

among the most prominent symptoms of the disease as it is common, but rather the loss of the sense of taste and smell. 65% of those who tested positive for the virus lost the sense of smell, compared to 21% of those who tested negative [17]

"Spector" believes that combining this prediction of artificial intelligence with the widespread spread of the smart application can help identify those who are likely to be spreaders of infection, as soon as the early symptoms appear on them, and help efforts to track new cases [13].

Conclusions and Discussion

Even with some early evidence, there are still many unanswered questions why do some people get well within a few weeks while others do? Will COVID-19 cause permanent odor loss for some people? Is the virus move out from the olfactory system to the brain? Loss of smell may be one of the symptoms of Covid-19 infection, however, most of the infected patients also suffer from fever, chills, fatigue, psychological distress, chest pain and stomach problems, and most of the symptoms do not appear to come directly from the virus, but from the body's excessive immune response to fight Virus. Experts indicate that the place with the highest intensity of the Coronavirus is not usually found in the lungs, but in the upper respiratory tract, especially in the nose and nasopharynx. This means that leaving your nose uncovered in the midst of the Corona virus outbreak exposes you to a double risk, as it allows the virus to enter a point of entry into your body, and also exit from it to infect others. The use of widely available smartphone applications in the fight against the current pandemic has a role in health-care institutions and health service providers to quickly identify people infected with the virus, especially with regard to identifying the loss of sense of smell and taste as the most prominent symptom of Corona.

References:

1. Symptoms of coronavirus. US Centers for Disease Control and Prevention website. Accessed May 8, 2020. https://www.cdc.gov/ coronavirus/ 2019-ncov/symptoms-testing/symptoms.html

2. World Health Organization https://www.who.int/ar/home

3. https://www.niaid.nih.gov/.

4. https://www.nationalgeographic.com/science/2020/08/thousands-covid- 19-patients-lost-sense-smell-will-get-back-cvd/

5. Whitcroft KL, Hummel T. Clinical diagnosis and current management strategies for olfactory dysfunction: a review. JAMA Otolaryngol Head Neck Surg. 2019; 1:1-9. doi:10.1001/jamaoto.2019.1728.

6. Hopkins C, Kumar N. Loss of sense of smell as marker of COVID-19 infection: joint statement from the British Rhinological Society and ENT-UK. Published March 21, 2020. Accessed April 5, 2020. www.entuk.org.

7. Claire Hopkins, Nirmal Kumar, Loss of sense of smell as marker of COVID-19 infection, www.entuk.org/sites/default/ files/files/ Loss % 20of%20sense%20of%20smell%20as%20marker%20of% 20 COVID .pdf

8. https://www.hopkinsmedicine.org/health/conditions-and-diseases/ smell-and-taste-disorders.

9. https://arabic.cnn.com/health/article/2020/04/12/loss-smell-and-taste-early-coronavirus-symptoms

10. National Institutes of Health, https://www.nih.gov/about-nih/who-we-are/nih-leadership

11. Leah C. Beauchampa,b, David I. Finkelsteina, Ashley I. Busha, C‹ Andrew H. Evansd and Kevin J. Barnhama, Parkinsonism as a Third Wave of the COVID-19 Pandemic, Journal of Parkinson's Disease (2020) DOI 10.3233/JPD-202211.

12. Spinato G, Fabbris C, Polesel J, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA. Published online April 22, 2020. doi:10.1001/jama.2020.677

13. Whitcroft KL, Hummel T. Clinical diagnosis and current management strategies for olfactory dysfunction: a review. JAMA Otolaryngol Head Neck Surg. 2019; 1: 1-9. doi:10.1001/jamaoto. 2019.1728.

14. Olfactory Dysfunction in COVID-19 Diagnosis and Management Katherine Lisa Whitcroft, BSc, MBChB; Thomas Hummel, MD, American Medical Association, Clinical Review & Education, June 23/30, 2020, vol. 323, no. 24.

15. Daniele Borsetto, Evolution of loss of smell or taste in COVID-19, NEWS RELEASE 2-JUL-2020.

16. Neelaysh vukkadala, Eben Rosenthal, Zara M. patel, Response to COVID 19 and the Otolaryngologist: Preliminary Evidence Based Review. vol. 130, Issue10. October 2020, pp. E526-E526.

17. Patel, Zara, The evidence for olfactory training in treating patients with olfactory loss, Otolaryngology & Head and Neck Surgery: February 2017, vol. 25, Issue 1, pp. 43-46.

18. Katherine Lisa Whitcroft, BSc, MBChB; Thomas Hummel, MD, Olfactory Dysfunction in COVID-19 Diagnosis and Management, American Medical Association. June 23/30, 2020 Vol. 323, No. 24.

19. https://play.google.com/store/apps/details?id=com.joinzoe.covid_ zoe&hl=en_US.

20. Cristina Menni, Ana M. Valdes, Maxim B. Freidin, Carole H. Sudre, Long H. Nguyen, David A. Drew, Sajaysurya Ganesh, Thomas Varsavsky, M. Jorge Cardoso, Julia S. El-Sayed Moustafa, Alessia Visconti, Pirro Hysi, Ruth C. E. Bowyer, Massimo Mangino, Mario Falchi, Jonathan Wolf, Sebastien Ourselin, Andrew T. Chan, Claire J. Steves, Tim D. Spector, Real-time tracking of self-reported symptoms to predict potential COVID-19, Nature Medicine, vol. 26, (2020) pp. 1037–1040.


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