

## Research Article

Mohammed Kamal Nsaif\*, Bilal Adil Mahdi, Yusor Rafid Bahar Al-Mayouf, Omar Adil Mahdi, Ahmed J. Aljaaf, and Suleman Khan

# An online COVID-19 self-assessment framework supported by IoMT technology

<https://doi.org/10.1515/jisys-2021-0048>

received March 30, 2021; accepted July 04, 2021

**Abstract:** As COVID-19 pandemic continued to propagate, millions of lives are currently at risk especially elderly, people with chronic conditions and pregnant women. Iraq is one of the countries affected by the COVID-19 pandemic. Currently, in Iraq, there is a need for a self-assessment tool to be available in hand for people with COVID-19 concerns. Such a tool would guide people, after an automated assessment, to the right decision such as seeking medical advice, self-isolate, or testing for COVID-19. This study proposes an online COVID-19 self-assessment tool supported by the internet of medical things (IoMT) technology as a means to fight this pandemic and mitigate the burden on our nation's healthcare system. Advances in IoMT technology allow us to connect all medical tools, medical databases, and devices via the internet in one collaborative network, which conveys real-time data integration and analysis. Our IoMT framework-driven COVID-19 self-assessment tool will capture signs and symptoms through multiple probing questions, storing the data to our COVID-19 patient database, then analyze the data to determine whether a person needs to be tested for COVID-19 or other actions may require to be taken. Further to this, collected data can be integrated and analyzed collaboratively for developing a national health policy and help to manage healthcare resources more efficiently. The IoMT framework-driven online COVID-19 self-assessment tool has a big potential to prevent our healthcare system from being overwhelmed using real-time data collection, COVID-19 databases, analysis, and management of people with COVID-19 concerns, plus providing proper guidance and course of action.

**Keywords:** COVID-19 pandemic, healthcare systems, self-assessment service, IoMT, medical database

## 1 Introduction

It was anticipated that 2020 is the beginning of an exciting decade in which we thought that we are mature enough to face global challenges such as infectious diseases, global warming, space invasion, and yet others. Undoubtedly, the development of basic science and technology frameworks toward data intensive applications has improved in vital healthcare areas including neuroscience, genomics, pharmaceutical development, medical imaging, and many others [1–4]. Eminent big technology innovations such as IoT technology [5], digital and mobile health [6], big data methods [7], along with the advances in artificial

---

\* **Corresponding author: Mohammed Kamal Nsaif**, Department of Computer Sciences, College of Education for Pure Sciences-Ibn Al-Haitham, University of Baghdad, Baghdad, Iraq, e-mail: mohammed.k.n@ihcoedu.uobaghdad.edu.iq

**Bilal Adil Mahdi:** Ministry of Education, General Directorate of Education Al-Kharkh/Al-Awala, Baghdad, Iraq

**Yusor Rafid Bahar Al-Mayouf, Omar Adil Mahdi:** Department of Computer Sciences, College of Education for Pure Sciences-Ibn Al-Haitham, University of Baghdad, Baghdad, Iraq

**Ahmed J. Aljaaf:** Center of Computer, University of Anbar, Ramadi, Iraq

**Suleman Khan:** Department of Computer and Information Sciences, Northumbria University, Newcastle upon Tyne NE1 8ST, United Kingdom

intelligence and machine learning can work toward smart solutions to deliver essential insights into global challenges such as COVID-19 pandemics via managing people with COVID-19 concerns and unlocking modern therapeutic solutions [8–10].

Such inter-related technology innovations have a big potential for hospitals and clinical practices to establish a highly interconnected digital ecosystem, enabled by Internet of Things (IoT) technology for real-time data collection at scale, and empowered by machine learning and rule-based systems to comprehend big healthcare data and to discover trends, represent medical databases, modeling risks and predict outcomes [11–14]. The use of IoT technology for health and medicine is commonly referred to as the Internet of Medical Things (IoMT), is an integration of medical devices, medical databases, applications, and people connected to a healthcare information system via the internet [15–18]. A feasible network of healthcare services is enabled using the IoMT technology so that different medical services are interconnected through the applications of internet-based devices such as smart sensors and medical equipment [19,20].

The crucial role of IoMT technology comes into the picture when providing healthcare services to remote areas or managing a large number of people in a natural disaster and global pandemics such as the emerging COVID-19 [21]. Proper use of IoMT concepts and tools has a great potential to improve healthcare services and medical operations. Current IoMT and real-time rule-based systems can incorporate toward therapeutic data administration, portable medical care, and patients follow up [22–24].

While COVID-19 pandemic continues to propagate and the second wave is almost formulating, the Iraqi health sector appears to be unprepared to handle the increasing number of infections. The acute shortages of medical technology, ICU equipment, and the rapidly spreading virus has exacerbated the situation and overloaded our hospitals. Currently, there is no automated system for COVID-19 self-management or tracking patients who are self-isolated. The lack to reach all patients with COVID-19 concerns has resulted in missing national collaborative emergency network, and thus we must push forward using innovative IoT-based applications of self-management empowered by a rule-based approach to help contain COVID-19 pandemic.

In this study, we have formulated a consensus version of COVID-19 self-assessment supported by clinicians with rich experience from different Iraq cities. As of 28 March 2021, more than 822,000 COVID-19 cases and 14,157 deaths were confirmed in Iraq [25]. It is anticipated that Iraqi hospitals to overwhelm with huge numbers of COVID-19 patients, while our healthcare system is highly likely to collapse due to this pandemic. Patients can simply include their health status, i.e. signs and symptoms, to the IoMT-based platform. The data goes through our COVID-19 patient database via the online COVID-19 self-assessment tool, then the data can be managed and analyzed using the embedded rule-based approach. Early diagnostic will be suggested, and hospitalization alert will automatically be generated for reference. Further treatment recommendations can be made as per the feedback from the prior analysis of data that are already stored in the database.

This paper is organized as follows; Section 2 focuses on some countries that have managed to mitigate the spread of the disease. Section 3 describes our framework providing a full picture of the components as well as how these components are collaborating. Subsections within Section 3 present different components and their functions. Section 4 covers the evaluation of our proposed framework as an interaction system, in which a cognitive walkthrough has been applied to help identify usability issues. Section 5 describes the most important findings and the strengths and limitations. Section 6 highlights the importance of using combined technology of IoMT with the rule-based approach toward patient-centric systems as a means to improve our healthcare quality of service.

## 2 Related works

Today, 196 countries, including Iraq, are still looking for cost-effective and practical solutions to confront the outbreak of COVID-19. Healthcare authority in Taiwan has predicted to have a greater number of COVID-19 infections, and therefore they started to specify several methods for many possible pathways including

early COVID-19 identification, suppression, and resource provision to guard the community. Taiwan has also integrated its national health insurance database to data from the immigration department as a means of starting big data analysis to generate real-time warnings based on travel history and clinical signs and symptoms. Further to this, they have made use of the latest technology including QR scanning codes, integrated reporting of transport history, and yet others for possible early detection of COVID-19 cases [26]. Similarly, healthcare authority in India has launched “ArogyaSetu” a smartphone application to establish links between people and important healthcare services [27].

Depending on discussions among government agencies and healthcare professionals, the spread of the virus has been reduced in South Korea by adopting and integrating several strategies. They adopted an approach called the 3T, which is the abbreviation for Trace, Test, and Treat [28,29]. The IoMT is essentially applied in the “Trace” strategy.

In technology, the most innovative country is Germany. A smartwatch application has been launched in Germany to reduce the spread of the virus and to detect infections. The vital signs (e.g., sleeping time, heart rate, and body temperature) are collected from people wearing the smartwatch in order to predict if they are infected with virus. An online map is used by the health authorities to access the collected data in order to assess the spread of infections [30]. Furthermore, a fast diagnostic device has been developed by Bosch to confirm COVID-19 infection hour by hour (as opposed to produce the outcomes in days). Rapid identification and isolation of infected people can be fulfilled by using the device, and then, mitigate the spread of the infections.

### 3 Framework design

The proposed framework assumes that it is possible to mitigate the problematic situation represented by COVID-19 pandemic, and there is an urgent need to utilize the facilities offered by the IoMT methodology supported by the rule-based approach for patients’ management. The core services of the framework proposed herein, shown in Figure 1, consist of the registration (personal – identifiable data), online consultation, storing the consultation data in COVID-19 patients database, COVID-19 diagnosis, and recommended alert service based on the provided diagnosis. This section discusses the design of these services. As mentioned previously, we propose an IoMT framework-driven online COVID-19 self-assessment tool. An alert service requires an automatic reaction at the diagnosis terminal when a COVID-19 alert rises. To control the spread of disease, it is important to report, identify, isolate, and handle the persons at early stages. Our proposed framework can be divided into the following main services.

#### 3.1 Registration and online consultation

The proposed framework starts with user registration, in which patients with COVID-19 concerns must register their necessary information such as their names, ages, genders, and contact information to gain access to the online self-assessment. Patient’s information will be securely stored in the COVID-19 database center for further analysis and assessment. Patients also need to report their signs and symptoms that are stored beside patients’ demographic for mining and knowledge discovery. The initial assessment of patient’s health status will go through our rule-based approach to match their signs and symptoms against the predefined rules.

Remote consultations have been adopted to minimize the infection risk, unnecessary visiting of hospitals, and the burden on healthcare systems. The online consultation service consists of five sets of separate tests, at the end of each test, patients are derived to the next one according to their answers. It is possible that the patients can be diagnosed at the first test, and thus there is no need to transfer them to the next test.

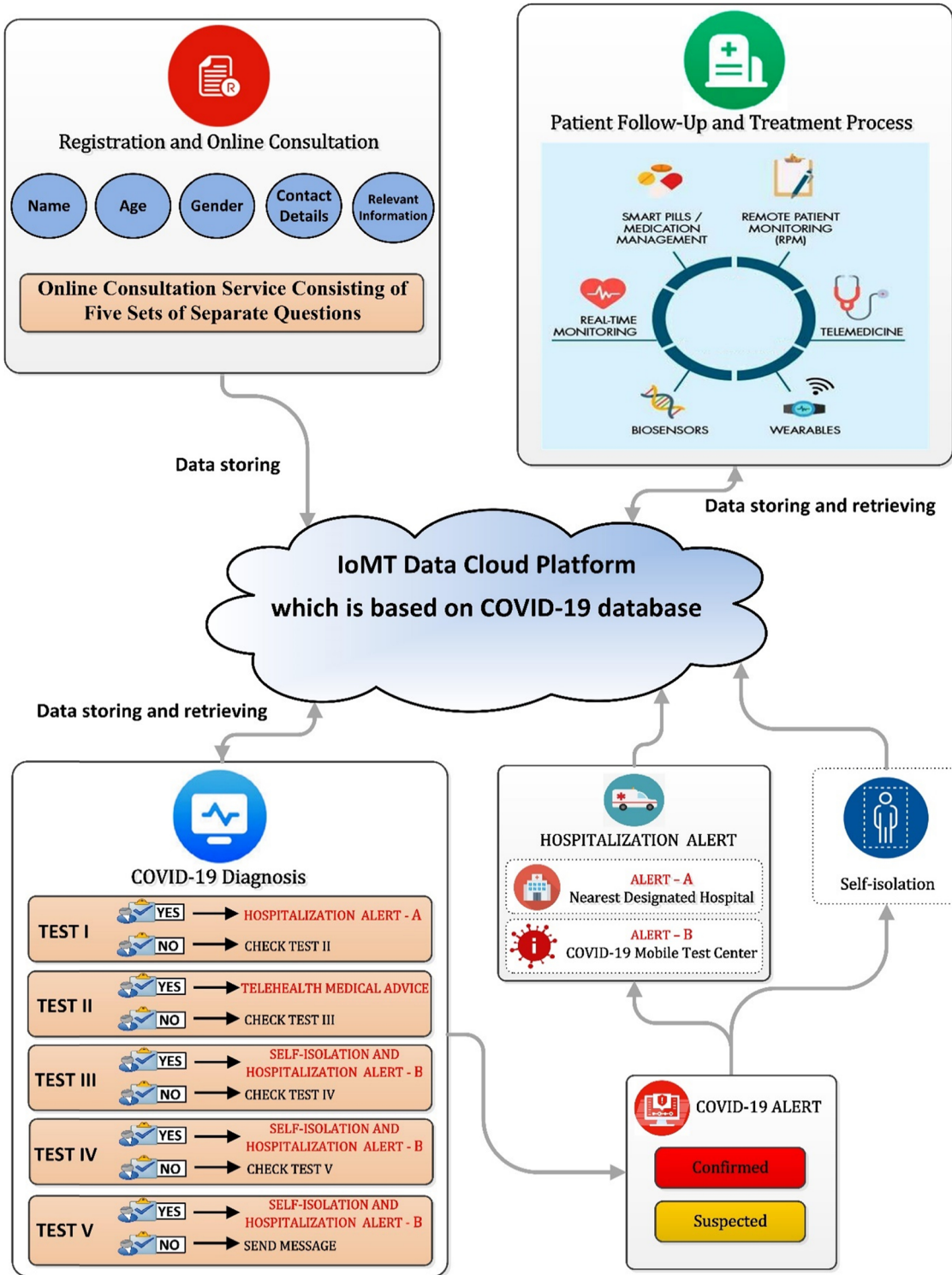


Figure 1: The proposed framework.

All the collected data from the online consultation service will also be persisted, i.e., the collected data are sent back to COVID-19 database for further management and analysis.

### 3.2 COVID-19 database

A centralized multidimensional database was designed in accordance with our framework requirements to securely hold patients' demographics, signs, and symptoms. It is one of the most important pillars in the workflow process of IoMT system as data from the online consultation will be stored in a patients cloud database server, which can be accessed by software components from each service within our framework, such as COVID-19 diagnosis service or the online consultation.

### 3.3 Diagnosis

This is a multistep process guiding patients with COVID-19 concerns through a validated rule-based self-assessment method to help determine whether patients with concerns need to be tested for COVID-19. Anyone with COVID-19 concerns can complete this self-assessment for him/herself or on behalf of somebody else if they are not able to do so. This self-assessment can inform the patients whether they have COVID-19 at the time of the test, even if they are not showing any symptoms. The self-assessment is not designed to detect previous infection with COVID-19. Also, it cannot check whether a person has any immunity to COVID-19. Figure 2 shows the self-assessment service that consists of five steps. Each step contains three actions, the first action represents a set of questions (TEST). The second action represents a condition. The third action represents what the patient has to do when the result of the condition is "Yes," and when the result is "No," the patient continues to the next step. As presented in Figure 2, the self-assessment method starts with test 1, which is a set of questions within our rule-based approach examining the presence of severe chest pain, difficulty breathing, feeling confused, or losing consciousness. Then according to answers, patient may be advised to continue to step 2 or shall go directly to the nearest emergency department via showing red alert as presented in Figure 2.

When patients continue to step 2, they are examined for any shortness of breath at rest or when laying down, in addition to any current respiratory chronic conditions. In this step, patients may encourage to contact healthcare professionals seeking advice with regard to their current symptoms (yellow alert), or continue their self-assessment and move forward to step 3, in which patients will be examined for any new cough, onset fever, shortness of breath, runny nose, and sore throat within the past 10 days. Yellow alert will also be issued when patients show any combination of two or more symptoms, in which they are asked to immediately self-isolate and be tested for COVID-19. Otherwise, they are encouraged to continue the self-assessment at step 4.

In step 4, patients are checked for the presence of painful swallowing, fatigue, achy muscle and joint, headache and stuffy nose, vomiting, nausea, and diarrhea, and finally losing the sense of taste or smell. When patients show combination of any two or more systems, they are strongly recommended to stay home and practice social distancing until they feel better (yellow alert). It is also advised that patients need to be tested for COVID-19 at this stage. The step 5 in this self-assessment, patients need to declare any outside travel in the last 14 days, or did they have close contact with somebody who is confirmed as having COVID-19. If so, they are advised to immediately self-isolate and to be tested for COVID-19. At the end of this multistep process, participants are advised to take part in asymptomatic testing and help to raise public awareness of social distancing and self-hygiene.

## 4 Cognitive walkthrough assessment

In this section, a cognitive walkthrough method has been applied to assess our framework as the seed of an interaction system and to help identify issues of usability [31]. To define problems in the design stage, the walkthrough is typically completed by several expert participants; however, this may also be achieved at the testing stage. The walkthrough method should be considered with a first-time user and focusing on the



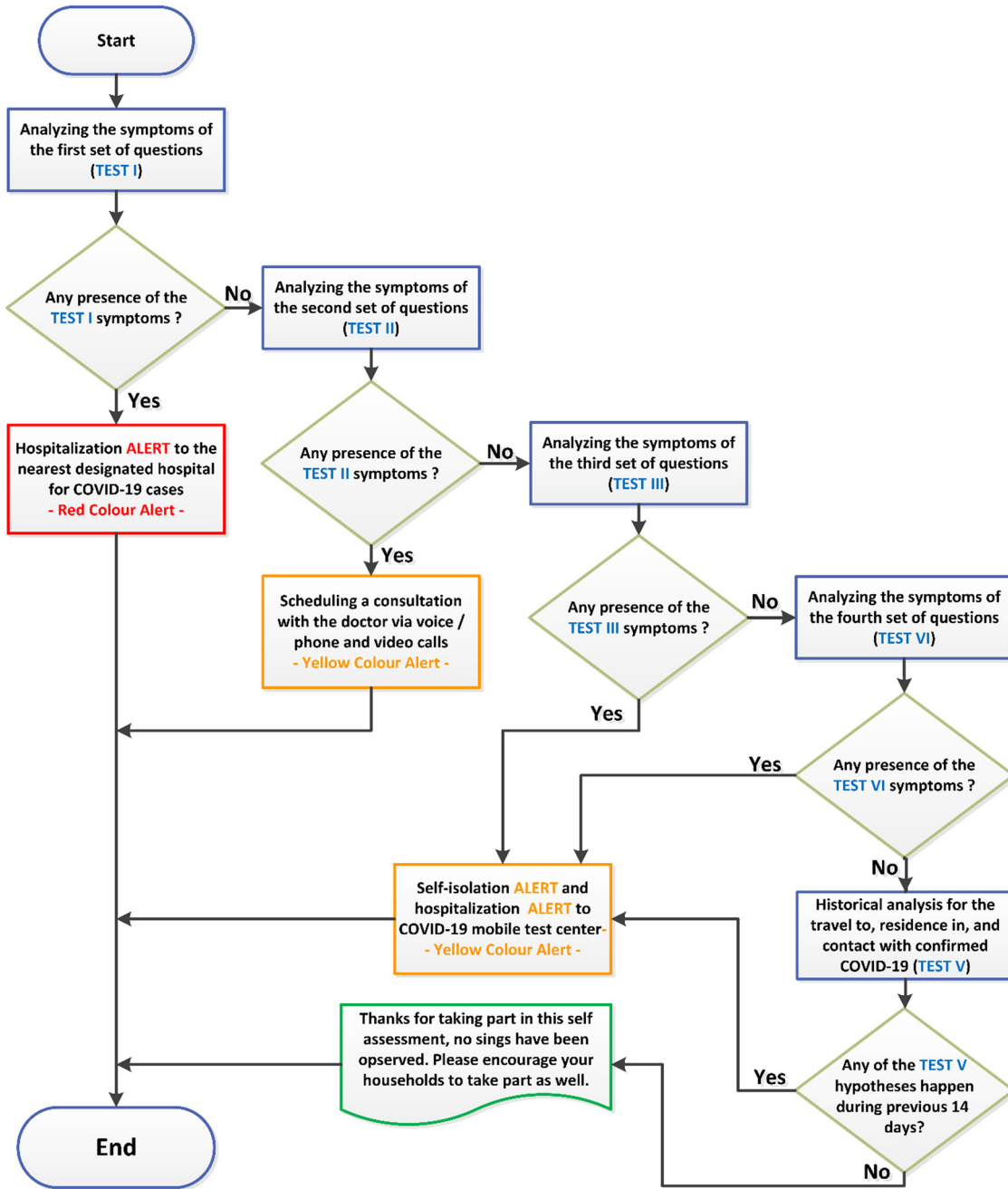


Figure 2: COVID-19 self-assessment service.

usability of the system. Four questions are required to be discussed by the cognitive walkthrough method during identifying task analysis and thereafter completed taking into consideration some pre-specified questions, including the following tasks.

- (1) User enrolment
- (2) Signs and symptoms
- (3) Alerts
- (4) Decision support

Each task will then be performed by the participants in order to answer the following questions, which are explained in detail in Table 1.

**Table 1:** A cognitive walkthrough assessment process

	Q1	Q2	Q3	Q4
User enrolment	To enroll new participant to use our framework, the participant must identify their demographic information first, then clarifying their signs and symptoms. They must start answering questions with related health status and this could be repeated later on using the same username and password	Participant login details will be securely kept for future use, especially having COVID-19 pre-assessment can be done regularly. Additionally, the framework is designed in a user-friendly approach to ensure proper help and guidance are provided to participants with different backgrounds. This will help the recognizability and learnability of the framework	Labels and terminology will be standardized and include the true language form to define the stages clearly within the framework	This framework ensures that participants will be provided with correct enrolment information when required, especially when participant inserts incorrect login details. On the access, the participant will be directed again to have another COVID-19 assessment
Signs and symptoms	For a participant, all relevant information and supporting decisions will be readily available online and stored in our data center	Once participant has logged in, the proposed framework will collect all signs and symptoms in a clear step-by-step manner, in which the participant does not be required to do anything else	All signs and symptoms will be standardized and contain the correct terms using a proper language to clearly capture what is happening to the participant	Participant at each visit can add new records to his/her profile, which includes historical logs as well as updated data in real time
Alerts	The participant will be noticed and alerted once signs and symptoms match one of the predefined tests	The proposed framework provides clear steps to complete the form, also steps from one step to another depend on data entry from participant	All alerts will also be standardized and contain the correct terms and proper language to clearly guide the participant to what they need to do	To prompt the participant of a potential COVID-19 infections, alert box prompts will be issued to guide for the next step. Each alert will clearly explain the situation and also the required action
Decision support	For health administrators who need to have access to the initial decision, they will be granted the list of signs and symptoms along with the decision for their reference	Decision labels will be clearly stated and highly descriptive so a participant can observe the true action to be taken	All decision labels will be standardized to a proper terminology using a proper language to clearly identify what action should be taken and which health service providers should be visited	Participant will receive feedback about details of their signs and symptoms along with the decision and action

- (1) Will the participants attempt to fulfill the correct effect?
- (2) Will the participants observe the true action is obtainable?
- (3) Will the participants connect the true action with the effect to be fulfilled?
- (4) If the true action is fulfilled, will the participants observe that is any progress may support the solving of the task?

## 5 Discussion

The use of IoMT technology has already altered the way in which online services are accessed, communicated, and delivered. IoMT along with rule-based approach can potentially bridge the gap of traditional patient/doctor consultations as well as improve healthcare delivery. Our framework provides a means of online consultation and diagnosis supported by IoMT technology and rule-based method for patients with COVID-19 concerns. This means individuals with concerns could have access to an authenticated medical procedure for COVID-19 diagnosis whilst at home or on the move, rather than having to take an appointment in medical centers or hospitals. Additionally, highlighted in the framework of this paper once a patient started to fill in signs and symptoms, there will be several assessment stages combined with multilevels of alert.

One of the proposed framework limitations is the inability to detect previous infection with COVID-19. Also, it cannot check whether somebody has any immunity to COVID-19. But on the other hand, this framework does not have an increased timeframe with respect to the accessibility and gathering of required information. Also, this framework is designed to save patients time in comparison to traditional methods of visiting hospitals while ensuring safety and reduce the need to collect tens of people with concerns at the same place. This shows that the framework offers both efficiency and effectiveness of managing patients/doctor interaction particularly for those at the front line of this pandemic. This positive outcome will therefore persuade all individuals with COVID-19 concerns to use our framework when becomes a stand-alone online system with a regular basis and possesses an appropriate experiment doing so.

## 6 Conclusion

In this paper, we present an integration of two innovative concepts: real-time data integration and analysis and IoMT technology. The use of these two paradigms for healthcare system can promote the crucial step forward for the adoption of self-assessment tool as a means for the management of COVID-19 pandemic. Our national healthcare system in Iraq is not well prepared to sustain such a huge number of daily infections along with the increasing demand for helpful care services to identify symptoms and provide guidelines for people with COVID-19 concerns. This was the main reason that pushed us to propose this feasible and scalable solution to allow users (patient, physician, and hospital management) to take advantage of this framework without the need of understanding complex standards or programming contexts. Our framework has been designed to analyze patients' input and propagate a response for the next action to be taken by the patient. The red alert represents that the patient should report to the COVID-19 treatment facility or nearest hospital with immediate effect, while the yellow indicates that the patient is highly likely exhibiting above 80% of COVID-19 signs and symptoms, thus should be screened and further assessment is crucial. Finally, no alert is presented when a patient does not show any symptoms at all. For future work, we plan to integrate our framework with a physical sensor device like smartwatch to provide easier and faster solution for the COVID-19 patients. Moreover, it is necessary to build a national Iraqi healthcare information system based on IoMT to support any framework that may be designed to overwhelm any health problems with huge numbers of patients.



**Acknowledgement:** The authors would like to acknowledge the editor-in-chief and managing editor for providing editorial support. We also gratefully thank the anonymous referees for their valuable comments and constructive suggestions.

**Conflict of interest:** Authors state no conflict of interest.

## References

- [1] Ahmed Z, Mohamed K, Zeeshan S, Dong X. Artificial intelligence with multi-functional machine learning platform development for better healthcare and precision medicine. *Database*. 2020;2020:1–35.
- [2] Alloghani M, Al-Jumeily D, Aljaaf AJ, Khalaf M, Mustafina J, Tan SY. The application of artificial intelligence technology in healthcare: a systematic review. *International Conference on Applied Computing to Support Industry: Innovation and Technology*. Cham: Springer; 2019. p. 248–61.
- [3] Andreu-Perez J, Poon CC, Merrifield RD, Wong ST, Yang G-Z. Big data for health. *IEEE J Biomed health Inform*. 2015;19:1193–208.
- [4] Jamil F, Ahmad S, Iqbal N, Kim D-H. Towards a remote monitoring of patient vital signs based on IoT-based blockchain integrity management platforms in smart hospitals. *Sensors*. 2020;20:2195.
- [5] Mahdi OA, Wahab AWA, Idris MYI, Znaid AA, Khan S, Al-Mayouf YRB. ESAM: endocrine inspired sensor activation mechanism for multi-target tracking in WSNs. *Fourth International Conference on Wireless and Optical Communications*; 2016. p. 99020B.
- [6] Lakhan A, Mohammed MA, Rashid AN, Kadry S, Panityakul T, Abdulkareem KH, et al. Smart-contract aware ethereum and client-fog-cloud healthcare system. *Sensors*. 2021;21:4093.
- [7] Abd Ghani MK, Noma NG, Mohammed MA, Abdulkareem KH, Garcia-Zapirain B, Maashi MS, et al. Innovative artificial intelligence approach for hearing-loss symptoms identification model using machine learning techniques. *Sustainability*. 2021;13:5406.
- [8] Bragazzi NL, Dai H, Damiani G, Behzadifar M, Martini M, Wu J. How big data and artificial intelligence can help better manage the COVID-19 pandemic. *Int J Environ Res public Health*. 2020;17:3176.
- [9] Kamal M, Aljohani A, Alanazi E. IoT meets COVID-19: status, challenges, and opportunities. *arXiv preprint arXiv:2007.12268*; 2020.
- [10] Singh RP, Javaid M, Haleem A, Suman R. Internet of things (IoT) applications to fight against COVID-19 pandemic. *Diabetes Metab Syndr Clin Res Rev*. 2020;14:521–4.
- [11] Latif AI, Daher AM, Suliman A, Mahdi OA, Othman M. Feasibility of internet of things application for real-time healthcare for Malaysian pilgrims. *J Comput Theor Nanosci*. 2019;16:1169–81.
- [12] Aljaaf AJ, Mallucci C, Al-Jumeily D, Hussain A, Alloghani M, Mustafina J. A study of data classification and selection techniques to diagnose headache patients. *Applications of big data analytics*. Cham: Springer; 2018. p. 121–34.
- [13] Ndiaye M, Oyewobi SS, Abu-Mahfouz AM, Hancke GP, Kurien AM, Djouani K. IoT in the wake of COVID-19: a survey on contributions, challenges and evolution. *IEEE Access*. 2020;8:186821–39.
- [14] Pham Q-V, Nguyen DC, Huynh-The T, Hwang W-J, Pathirana PN. Artificial intelligence (AI) and big data for coronavirus (COVID-19) pandemic: a survey on the state-of-the-arts; 2020. <https://www.preprints.org/manuscript/202004.0383/v1>.
- [15] Singh RP, Javaid M, Haleem A, Vaishya R, Al S. Internet of medical things (IoMT) for orthopaedic in COVID-19 pandemic: roles, challenges, and applications. *J Clin Orthop Trauma*. 2020;11(4):713–7.
- [16] Swayamsiddha S, Mohanty C. Application of cognitive internet of medical things for COVID-19 pandemic. *Diabetes Metab Syndr Clin Res Rev*. 2020;14(5):911–5.
- [17] Yang T, Gentile M, Shen C-F, Cheng C-M. Combining point-of-care diagnostics and internet of medical things (IoMT) to combat the COVID-19 pandemic. *Diagn*. 2020;10(4):224.
- [18] Khalid M, Awais M, Singh N, Khan S, Raza M, Malik QB, et al. Autonomous transportation in emergency healthcare services: framework, challenges, and future work. *IEEE Internet Things Mag*. 2021;4:28–33.
- [19] Aman AHM, Hassan WH, Sameen S, Attarbashi ZS, Alizadeh M, Latiff LA. IoMT amid COVID-19 pandemic: Application, architecture, technology, and security. *J Netw Comput Appl*. 2020;174:102886.
- [20] Mohammed MA, Elhoseny M, Abdulkareem KH, Mostafa SA, Maashi MS. A multi-agent feature selection and hybrid classification model for Parkinson's disease diagnosis. *ACM Trans Multimid Comput Commun Appl*. 2021;17:1–22.
- [21] Lin B, Wu S. COVID-19 (coronavirus disease 2019): opportunities and challenges for digital health and the internet of medical things in China. *Omics*. 2020;24:231–2.
- [22] Clark A. Can internet of medical things improve capabilities for COVID-19 treatment and reduce transmission of the disease? *Am J Med Res*. 2020;7:57–63.

- [23] Jain S, Nehra M, Kumar R, Dilbaghi N, Hu TY, Kumar S, et al. Internet of medical things (IoMT)-integrated biosensors for point-of-care testing of infectious diseases. *Biosens Bioelectron.* 2021;179:113074.
- [24] Zhang T, Liu M, Yuan T, Al-Nabhan N. Emotion-aware and intelligent internet of medical things towards emotion recognition during COVID-19 pandemic. *IEEE Internet Things J.* 2020. doi: 10.1109/JIOT.2020.3038631.
- [25] World Health Organization. <https://www.who.int/countries/irq/>; 2021 Mar 28.
- [26] Hui M. How Taiwan is tracking 55,000 people under home quarantine in real time. <https://qz.com/1825997/taiwan-phone-tracking-system-monitors-55000-under-coronavirusquarantine/>. Last accessed on 8, 2020.
- [27] Bassi A, Arfin S, John O, Jha V. An overview of mobile applications (apps) to support the coronavirus disease 2019 response in India. *Indian J Med Res.* 2020;151:468.
- [28] Leite H, Gruber T, Hodgkinson IR. Flattening the infection curve—understanding the role of telehealth in managing COVID-19. *Leadersh Health Serv.* 2020;33(2):221–6.
- [29] Sönmez G, Celik E. Digital fight against covid-19 and the “new normal” for security institutions. *Ankara: ORSAM;* 2020;247. p. 1–19.
- [30] Busvine D. Covid-19: Germany launches smartwatch app to monitor coronavirus spread. *The Star.* 2020. <https://www.thestar.com.my/tech/tech-news/2020/04/07/covid-19-germany-launches-smartwatch-app-to-monitor-coronavirus-spread>. Last accessed on 28 July 2021.
- [31] Mahatody T, Sagar M, Kolski C. State of the art on the cognitive walkthrough method, its variants and evolutions. *Intl J Human Comput Interact.* 2010;26:741–85.