Towards establishment of diagnostic reference levels based on clinical indication in the state of Qatar

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**HIGHLIGHTS**
- This is the first study in the Asian region and one of the very few that established DRLs based on clinical indication for CT.
- Standardized CI nomenclature must be established as there are no guidelines for accurate comparison between studies on CT patient exposure.
- The established clinical DRL values for CT will further facilitate patient dose optimization and quality improvement process HMC in Qatar.

**ABSTRACT**

Objectives: The objectives of this study were to: 1) evaluate patient radiation exposure in CT and 2) establish CT Diagnostic Reference Levels (DRLs) based on clinical indication (CI) in Qatar.

Materials and Methods: Patient data for 13 CIs were collected using specially designed collection forms from the dose management software (DMS) of Hamad Medical Corporation (HMC), the main Qatar healthcare provider. The methodology described in the International Commission on Radiological Protection (ICRP) Report 135 was followed to establish national clinical DRLs in terms of Volumetric Computed Tomography Dose Index (CTDIvol) and total Dose Length Product (DLPt). Effective dose (Ef) was estimated by DMS using DLPt and appropriate conversion factors and was analyzed for comparison purposes.

Results: Data were retrospectively collected for 896 adult patients undergoing CT examinations in 4 hospitals and 7 CT scanners. CT for Diffuse infiltrative lung disease imparted the lowest radiation in terms of CTDIvol (5 mGy), DLPt (181 mGy.cm) and Ef (3.6 mSv). Total body CT for severe trauma imparted the highest DLPt (3137 mGy.cm) and Ef (38.6 mSv) of all CIs with a CTDIvol of 15 mGy. Rounded Third quartile CTDIvol and DLPt values were defined as the Qatar CT clinical DRLs. Comparison was limited due to sparse international literature. When this was possible data were lower or comparable with other studies.

Conclusions: This is the first study reporting national clinical DRLs in Asia and second one internationally after UK. For accurate comparison between studies, systemized CI nomenclature must be followed by researchers.

1. Introduction

Medical imaging is a particularly important tool that helps the referring physician answer not only simple but also multiple complex clinical questions that were not possible to answer previously. The evolution of medical technology is facilitating this procedure. For example, CT has experienced a vast technology evolution the last decade. The industry offers multi-detector CT system up to 640 data...
channels for quicker scanning that is important for special group of patients such as paediatric patients (for reduction of motion artifacts or radiation dose) or for cardiac studies (for reduction of blur due to heart motion or breathing). New CT detector technology is introduced into the market that enables lower electronic noise and produces higher quality images or enables dual-energy spectral imaging. Furthermore, evolution in computer power enabled rapid use and growth of iterative image reconstruction algorithms with enormous possibilities in radiation dose reduction [1]. All this evolution of CT technology has revolutionized the pathway of patient diagnosis and treatment but still comes at the expense of radiation exposure. The latest NCRP 184 report published in 2019, that updates medical radiation exposure information with data collected between 2006 and 2016, states that still today Computed Tomography (CT) scanning is the largest contributor to collective effective dose [2].

In the last 20 years, radiation dose optimization in medical exposure and specially in CT has been strongly supported by many international standards such as International Basic Safety Standards (BSS) [3] and European BSS [4] and also by the International Commission on Radiological Protection (ICRP) [5-7]. For best optimization process, the term Diagnostic Reference Level (DRL) defines an indicative dose level that is not expected to be exceeded under normal conditions for a given clinical indication [3,4,7]. DLRs should be set by a professional society, regulatory authority or the ministry of health in each country, at a national level or by a European consortium or an International Organization [7]. Historically, the establishment and use of DRLs was common in Europe for the last 20 years. Also, recently the use of DRL has been strengthened and has become mandatory due to latest European legislation [8]. The latest ICRP 2017 report entitled “Diagnostic Reference Levels in Medical Imaging” [7] suggests defining DRLs for selected medical imaging tasks thus for a specific clinical purpose or indication.

DRLs in the international literature are mostly set for certain anatomical regions [9,10]. The limitation of anatomical DRLs, however, is that for one anatomical region of the patient body more than on clinical indication (CI) is applicable. Each of these CIs require quite different CT protocols to answer the clinical question with quite different patient radiation exposure. The last few years, the term clinical DRLs is introduced with limited number of studies defining DRLs in terms of CI [11-14]. Also, recently a European Project was funded by the European Commission with the aim to define DRLs for the most important clinical indications across Europe [15].

Despite these efforts there is scarce information published in the recent international literature on national clinical DRLs. The objectives of this study were to 1) evaluate patient radiation exposure in various CT procedures based on CI and 2) establish CT DRLs for the most important CIs in the State of Qatar.

2. Materials and methods

The state of Qatar is not a big country compared to other countries of the world. The current population of Qatar is 2,866,397 as of Sunday, March 15, 2020, based on Worldometer elaboration of the latest United Nations data [16]. However, the last years, the state has witnessed rapid population growth mainly due to migrant workers employed in the construction industry, primarily to fulfill the requirements of rapid infrastructure development for the 2022 FIFA World Cup [17]. The Qatari population is 15 % of Qatar’s total population. The remaining 85 % is made up of a workforce of over a hundred different nationalities (Arab, Indian, Filipino, Nepali, Bangladeshi, Sri Lankan and others) with Indians constituting the largest group of expats in Qatar [17]. Ninety-six percent (96 %) of population is urban with a median age of 32.3 years, mainly being Asian. As stated above, it consists of expats that come to the country for work. Due to a huge influx of male workforce, women account for just 25 % of the population. Thus, Qatari population is distinctive with considerable percentage of noticeably young male inhabitants coming from other countries of the world.

Health care services in Qatar are provided mainly through the Ministry of Public Health. Basic health care is provided free of charge to all residents including expatriates. Hamad Medical Corporation (HMC) is the main secondary and tertiary healthcare provider in the state of Qatar and one of the leading hospital providers in the Middle East. HMC’s network is made up of 13 hospitals – nine specialist hospitals and four community hospitals as well as the national Ambulance Service, home and residential care and mental health service. HMC bed capacity as of 2019 statistics is 2773 with over 350,000 patients carried out across HMC emergency department, various outpatient departments and day care, radiology and dialysis units, Hamad Medical Corporation is the largest non-profit healthcare provider in Qatar, providing around 90 percent of acute services in the country http://www.acertus.co.uk/interest/about_hmc.html.

The data were collected retrospectively for the period of 2018–2019 from 7 CT scanners installed during the years 2005–2017. The CT systems were from one manufacturing company (Siemens Healthineers AG, Frankfurt, Germany) and of 4 models (Somatom Definition Edge 128, Somatom Definition Flash 128 dual source, Sensation 64 and Somatom Definition As 64).

In the attempt to evaluate patient radiation exposure based on CI and establish CT clinical DRLs in the State of Qatar, a first meeting was held in February 2019 with representatives of respective HMC radiology departments, the HMC Radiation Safety Section and the Qatar Medical Physics Society. During this meeting, the CIs to focus were decided, chosen either because of high frequency in the state of Qatar or because of possible increased radiation exposure of patient (Table 1).

Collection forms were prepared in excel format during the meeting to facilitate data collection in a uniform manner and assist data analysis. The forms aimed to include patient demographic information and CT technical parameters (patient age, weight, kV, mAs, number of phases, etc.). It was decided to retrospectively collect data using the dose management software (DMS) (Radiation Dose Monitor, MPTronic Medical Systems, France) connected to the HMC picture archiving and communication system (PACS) (PACSHealth LLC, Scottsdale, AZ). Only adult patients (16+: years of age) would be included in the study. The dosimetric quantities provided by the CT scanners were Volumetric Computed Tomography Dose Index (CTD hurdle) and Dose Length Product (DLP). As the DMS could also estimate Effective dose (Ef), this dosimetric quantity was also collected from the DMS for analysis.

The study received ethical approval by the HMC Medical Research Center. For each hospital taking part in the study, the senior technologist was responsible for data collection and for answering any related questions. Data were collected anonymously; all identifiers were removed before sharing the data. For accurate establishment of CT clinical DRLs, the methodology described in International Commission on Radiological Protection (ICRP) Report 135 was strictly followed [7]. For body CT examinations where patient weight was known, patient sample included 20 patients of normal weight (70 ± 15 kg). For those CT examinations that patient weight was not known for any reason, a larger sample was collected (100 patients). Only CT exams with complete patient information were included. Finally, subjective image quality evaluation was made by qualified medical physicist using AAPM standard using the ACR phantom for each patient included in the survey to ensure that image quality of CT images was adequate to answer corresponding diagnostic question.

After data collection, a second meeting was held during which data were discussed, cleaned, typos were corrected, and clarifications were provided in order to proceed with data analysis. Once data cleaning was finalized, analysis was performed mainly using Microsoft Excel, Microsoft Corporation, 2018. The DRLs were defined as followed: 1) estimation of the median of each hospital for each CI and 2) estimation of the 75th percentile of all the medians for each CI.
The clinical indications (CIs), Hospital and CT scanner data are shown below for computed tomography (CT). These CIs are considered important for the state of Qatar.

| N  | CI                                        | Hospital                                      | Abbreviation Models       |
|----|-------------------------------------------|-----------------------------------------------|---------------------------|
| 1  | liver and abdominal metastases in colorectal cancer | National Center for Cancer Care Research | NCCCR SOMATOM Definition AS (64) |
| 2  | Appendicitis                              | Hamad General Hospital                        | HGH SOMATOM Definition Edge (128) |
| 3  | Chest-abdomen-pelvis oncologic follow-up   | National Center for Cancer Care Research       | NCCCR SOMATOM Definition AS (64) |
| 4  | Chronic sinusitis                         | Ambulatory Care Center                        | ACC SOMATOM Definition Flash (128) Dual source |
| 5  | Diffuse infiltrative lung disease         | Ambulatory Care Center                        | ACC SOMATOM Definition Edge (128) |
| 6  | Acute head trauma/Cervical spine trauma   | Hamad General Hospital                        | HGH SOMATOM Definition Flash (128) Dual source |
| 7  | Pulmonary embolism                        | Hamad General Hospital                        | HGH SOMATOM Definition Flash (128) Dual source |
| 8  | Total body CT in severe trauma            | Hamad General Hospital                        | HGH SOMATOM Definition Flash (128) Dual source |
| 9  | Urinary calculus                          | Hamad General Hospital                        | HGH SOMATOM Definition Edge (128) |
| 10 | Coronary artery disease                   | Heart Hospital                                | HH SOMATOM Definition Flash (128) Dual source |
| 11 | Chest pain                                | Heart Hospital                                | HH SOMATOM Definition Flash (128) Dual source |
| 12 | Stent                                     | Heart Hospital                                | HH SOMATOM Definition Flash (128) Dual source |
| 13 | pre TAVI evaluation                       | Heart Hospital                                | HH SOMATOM Definition Flash (128) Dual source |

### 3. Results

The study includes data retrospectively collected for 896 adult patients undergoing CT examination for a variety of CIs (13). The HMC hospitals and CT scanners included in the study are listed in Table 1.

According to the HMC policy, each patient is referred to a specific HMC hospital depending on the CI (general, cardiac, trauma center, etc). Thus, not all hospitals perform CT examinations for all CIs. The study included 4 specialized hospitals and 7 CT scanners based on the choice of CIs at the design phase of the study.

Table 2 shows patient and protocol data for CT. There seems to be no specific trend on patient age and CIs apart from the fact that for 8 out of 13 CIs, patients were under the age of 50 years and for 5 of them patients were in the range of 30–40 years (appendicitis, chronic sinusitis, urinary calculus, head/cervical and total body trauma). Taking into consideration the young population in the state of Qatar this was to be expected. The only CT exam that seemed to have more focused patient age (54–84 years of age, mean age 70 years) was for pre Transcatheter Aortic Valve Implantation (TAVI) evaluation. As far as gender distribution was concerned, female population reported started from 5 % for total body CT for severe trauma up to 55 % for pulmonary embolism. The low percentage of female patients for total body CT for severe trauma (5 %) could be attributed to male accidents happening at work (mainly construction site accidents). Due to the CT technology of the scanners included in the study CT protocols for all CIs adjusted manual technical parameters (kV and mAs) to tailor patient exposure and eventually image quality for each patient.

Table 3 presents patient dosimetric data for all CIs. As data did not follow a normal distribution, median and range of dosimetric data were estimated and shown for the 13 CIs for CT. The lowest radiation dose in terms of CTDIvol was reported for diffuse infiltrative lung disease (5 mGy) whereas the highest was reported for acute head trauma/Cervical spine trauma (38.4 mGy). Sixty two percent (62 %) of CIs had CTDIvol below 10 mGy. Out of the 13 CIs only 3 (chronic sinusitis, diffuse infiltrative lung disease and urinary calculus) were single phase exams. The rest were 2–5 phase examinations with oncologic follow up having the highest number of phases (max 5). As far as DLPt is concerned, again diffuse infiltrative lung disease had the lowest value (181 Gy.cm) whereas the highest value was reported for total body CT in severe trauma due to scan length (whole body) (3137 Gy.cm). Seventy percent (70 %) of CIs were below 1000 Gy.cm and 92 % below 1500 Gy.cm. Regarding the 4 cardiac CIs (coronary artery disease, chest pain, stent and pre TAVI evaluation) results showed that CTDIvol values were similar. DLPt followed same pattern in all CIs except the pre TAVI evaluation that had double DLPt value (671 mGy.cm) compared to the other 3 cardiac CIs (339–389 mGy.cm).

Finally, the lowest E was found for diffuse infiltrative lung disease (3.5 mSv) and the highest for total body CT in severe trauma (38.6 mSv). Fig. 1 presents the CIs and median Ef in ascending order. Most of the CT examination are below 10 mSv. The CIs that are related to oncological imaging and total body CT after severe trauma have Ef that is higher than 20 mSv. Although Ef is not a good indicator of risk for individual patients it is noted here for comparison purposes.

Table 4 presents the proposed DRLs of the state of Qatar for 13 predefined CIs in CT as the rounded 3rd quartile values of median CTDIvol and DLPt values of patient sample in each hospital and for each CI. These clinical DRLs values were endorsed by the Medical Physics Society of the state of Qatar and are in the implementation process to be approved by the regulatory authority.

### 4. Discussion

This is the first study reporting on national clinical DRLs in the country of Qatar and in the Asian region based on a broad number of CIs decided at a national level and based on national frequency and radiation dose optimization needs. The results were based on data retrospectively collected for 896 adult patients undergoing CT examination for a variety of CIs following the methodology described at the ICRP 135 report on “Diagnostic Reference Levels in Medical Imaging”. Data were collected from 4 hospitals and 7 CT systems of HMC, the main health care provider of Qatar. The use of the DMS installed at HMC enabled...
Table 2
Basic patient and protocol data in CT examinations.

| N  | Clinical indication                                          | % female patients | Mean age (years) | Age range (years) | kV range | mAs range |
|----|-------------------------------------------------------------|-------------------|------------------|-------------------|----------|-----------|
| 1  | Abdominopelvic CT for liver and abdominal metastases in colorectal cancer | 32                | 55               | 28–75             | 100–120  | 220       |
| 2  | Appendicitis                                                | 30                | 31               | 16–63             | 80–140   | 67–340    |
| 3  | Chest-abdomen-pelvis for oncologic follow-up                 | 50                | 57               | 25–79             | 100–120  | 220       |
| 4  | Chronic sinusitis                                            | 51                | 37               | 15–77             | 80–140   | 93–630    |
| 5  | Diffuse infiltrative lung disease                            | 48                | 51               | 18–93             | 80–120   | 38–260    |
| 6  | Acute head trauma/Cervical spine trauma                      | 24                | 32               | 16–119            | 100–140  | 168–501   |
| 7  | Pulmonary embolism                                           | 55                | 43               | 17–87             | 80–120   | 76–203    |
| 8  | Total body CT in severe trauma                               | 5                 | 30               | 17–75             | 80–140   | 97–712    |
| 9  | Urinary calculus                                             | 12                | 34               | 19–67             | 100–140  | 67–303    |
| 10 | Coronary artery disease                                     | 32                | 44               | 19–72             | 100–120  | 370       |
| 11 | Chest pain                                                   | 41                | 47               | 17–70             | 100–121  | 370       |
| 12 | Stent                                                        | 19                | 56               | 20–72             | 100–122  | 370       |
| 13 | Pre TAVI evaluation                                          | 50                | 70               | 54–84             | 100–123  | 370       |

CTDIvol: Volumetric Computed Tomography Dose Index.
DLPt: Total Dose Length Product.
Ef: Effective dose.
Npat: Number of patients.
Np: Number of CT phases.

Table 3
Patient dosimetric data for all CT CIs are shown.

| N  | Clinical indication                                          | Hospital | Npat | CTDIvol | DLPt | Ef   | Np |
|----|-------------------------------------------------------------|----------|------|---------|------|------|----|
| 1  | Abdominopelvic CT for liver and abdominal metastases in colorectal cancer | NCCCR   | 40   | 9.6 (5.3–23.2) | 1389 (739–3474) | 24.5 (13.4–59.8) | 3–4 |
| 2  | Appendicitis                                                | HGH     | 100  | 11.5 (6.5–38.1) | 562 (283–2080) | 8.1 (2.5–25.6) | 2  |
| 3  | Chest-abdomen-pelvis oncologic follow-up                     | NCCCR   | 40   | 10.4 (4.7–20.7) | 1427 (626–3045) | 26.1 (11.3–56.2) | 3–5|
| 4  | Chronic sinusitis                                            | ACC     | 100  | 30.2 (4.1–55.0) | 737 (117–1421)  | 6.9 (1.1–14.1)  | 1  |
| 5  | Diffuse infiltrative lung disease                            | ACC     | 97   | 5.0 (2.1–10.7)  | 181(83–393)     | 3.6 (1.3–7.5)   | 1  |
| 6  | Acute head trauma/Cervical spine trauma                      | HGH     | 100  | 38.4 (14.7–83.2) | 1347 (422–2990) | 3.6 (1.3–19.3)  | 1–2|
| 7  | Pulmonary embolism                                           | HGH     | 100  | 5.5 (2.1–13.2)  | 349 (121–775)   | 6.7 (2.4–15.7)  | 2  |
| 8  | Total body CT in severe trauma                               | HGH     | 100  | 14.5 (3.9–48.5) | 3137 (1467–6194) | 38.6 (13.8–87.4) | 3–4|
| 9  | Urinary calculus                                             | HGH     | 100  | 7.4 (2.5–23.0)  | 334 (128–1817)  | 5.0 (1.9–27.3)  | 1  |
| 10 | Coronary artery disease                                     | HH      | 40   | 6.8 (2.6–11.3)  | 354 (198–661)   | 5.0 (2.7–9.2)   | 3  |
| 11 | Chest pain                                                   | HH      | 39   | 6.7 (4.5–13.4)  | 389 (93–773)    | 5.4 (1.2–10.8)  | 3  |
| 12 | Stent                                                        | HH      | 21   | 6.8 (3.1–10.3)  | 339 (134–769)   | 4.7 (1.9–10.8)  | 4  |
| 13 | Pre TAVI evaluation                                          | HH      | 19   | 5.5 (1.0–10.0)  | 671 (378–1546)  | 12.5 (5.3–30.7) | 4  |

Fig. 1. Median Effective dose (Ef) values for the 13 clinical indications (CIs) are shown.
easy and uniform data collection. Apart from CTDIvol and DLPt the software also provided Ef and values were analyzed for comparison purposes. The results show that total body CT for severe trauma imparted the highest DLPt (31.37 mGy.cm) and Ef (38.6 mSv) of all CIs with a medium level values of CTDIvol (15 mGy). Diffuse infiltrative lung disease imparted the lowest radiation of all CIs in terms of CTDIvol (5 mGy), DLPt (181 mGy.cm) and Ef (3.6 mSv).

The attempt to compare clinical DRLs of Qatar with published national clinical DRLs in the recent international literature was limited as there was no other study providing data, for the same clinical indications. To our best knowledge, the only studies published in the international literature, reporting on national DRLs or reporting on national surveys based on CI were a) a UK study published in 2014 by the Public Health England [12], b) a national survey defining Swiss DRLs in 2010 [14] and c) one national French study published in 2019 reporting on patient dose evaluation on CT based on CI [11]. The study was undergone by Public Health England and reported on a UK national review of CT examinations performed in 2011 and determined UK DRLs for certain CIs. The Swiss survey was undertaken by the Swiss Federal Office of Public Health. The authors defined CT protocol national DRLs taking into consideration various CIs but not explicitly defining clinical DRLs (one DRL value could apply to more than once CIs). The French study was conducted by the French Society of Medical Physics (SFPM) on patients aged ≥16 years who underwent CT examinations in France between 2015 and 2017 in collaboration with French Society of Radiology (SFR) and its associated organ sections. The authors mentioned that their study could serve as an important tool for the French radiation protection authorities to update French DRLs (data reported were thus not the French national clinical DRLs). Fig. 2a and b present Qatar CT DRLs and values reported from these 2 studies. Comparison was not possible for all but only limited CIs. For pulmonary embolism, CTDIvol value of this study appeared to be lower than the UK, Swiss and French studies (Fig. 2a) whereas for chest pain values was 7 times less the Swiss study (possibly due to the recent CT technology evolution that allowed for substantial dose reduction in cardiac studies opportunities compared to 10 years ago). On the other hand, CTDIvol DRL for appendicitis and head/cervical fracture or trauma were slightly higher than the French study. It must be noted though that neither of these CIs were defined in a similar manner. For example, in the French study the CI was entitled as “AP/Pain” and included a number of CIs such as abdominal pain, suspicion of appendicitis and sigmoiditis, peritonitis or intestinal perforation, whereas the current study solely appendicitis was considered. The same was noticed for Head and neck trauma. The French study defined a CI with the title “Head trauma” as a traumatic brain injury and separately a CI called “neck trauma” as cervicobrachial neuralgia, neck pain or trauma. Obviously, direct accurate comparison was not possible for these CIs. As far as DLPt was concerned, Qatari DRL values were in general higher than the 3 European studies except chest pain. As there are no detailed data on, possibly due variation of CT clinical protocol. The main limitation related to this comparison appeared to be that nomenclature for CI was different between studies (Qatar, UK, Swiss and French study). To allow accurate comparison between studies in the future, a systemized, consistent methodology for CI nomenclature should be followed. Another important difference is that the three studies (UK, Swiss and French studies) were performed in much bigger countries than the State of Qatar and also in another continent with different patient demographics (European studies).

Regarding cardiac CIs there are limited number of studies published in the international literature reporting national DRLs. This appears to be the first study reporting national clinical DRLs for 4 cardiac CIs. In the attempt to compare patient dose results with recent published data it was realized that specifically for pre TAVI evaluation radiation dose reports were very limited. Talei Franzesi et al 2018 performed a dose optimization study and reported values of DLPt and Ef before (2044 mGy.cm and 28.82 mSv) and after (1600 mGy.cm and 22.56 mSv) optimization [17]. Their results were more than double the results of this study. A systematic review by Alhailiy AB et al. on cardiac CT angiography reported a big variation of cardiac CT angiography DRLs with range of 25–70 mGy on CTDI and 671–1510 mGy.cm on DLP [18], again higher than results in this study.

5. Conclusions

The current study is the first in the Asian region and one of the very few studies in the world that report on DRLs for 13 clinical indications in CT. The clinical indications were decided based on national frequency and optimization needs in the state of Qatar. The established clinical DRL values for CT will further facilitate patient dose optimization and quality improvement process within Hamad Medical Corporation and the state of Qatar.

Comparison with recent literature revealed that it was difficult or even impossible to identify similar clinical indications as no standard guidelines existed and authorities, institutions or authors of a study defined clinical indications and corresponding DRLs at will. For accurate, precise comparison between studies on CT patient exposure, a standardized CI nomenclature must be established.

Statistics and biometry

No complex statistical methods were necessary for this paper.

Informed consent

Written informed consent was not required for this study because no Human Subject.

Ethical approval

Institutional Review Board approval was obtained.

Study subjects or cohorts overlap

The study subjects or cohorts have not been previously reported.

Methodology

Retrospective.
Multicentre study / performed at one institution.

Guarantor

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Huda AlNaemi: Project administration, Conceptualization, Methodology, Writing - original draft, Visualization, Investigation, Supervision, Writing - review & editing. **Virginia Tsapaki**: Conceptualization, Methodology, Writing - original draft, Visualization, Investigation, Supervision, Writing - review & editing. **Ahmed J. Omar**: Visualization, Investigation, Writing - review & editing. **Maryam AlKuwari**: Visualization, Investigation, Writing - review & editing. **Amal AlObadli**: Visualization, Investigation, Writing - review & editing. **Shady Alkhazzam**: Data curation, Writing - review & editing. **Antar Aly**: Project administration, Conceptualization, Methodology, Writing - original draft, Visualization, Investigation, Supervision, Writing - review & editing. **Mohammad Hassan Kharita**: Conceptualization, Methodology, Writing - original draft, Visualization, Investigation, Supervision, Writing - review & editing.

Declaration of Competing Interest

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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