Radioprotection 2019, 54(3), 187–194

https://doi.org/10.1051/radiopro/2019019

Available online at:
www.radioprotection.org

ARTICLE

Establishment of age-specific reference levels and achievable doses for children and adults undergoing nuclear medicine exams

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Received: 14 July 2018 / Accepted: 3 May 2019

Abstract – Reference levels (RLs) and achievable doses (ADs) have been investigated for routine nuclear medicine and molecular imaging procedures across various hospitals. The RLs and ADs were then set at 75th and 50th percentile of the data collected respectively. The minimum and maximum administered activities (in MBq) were asked for ^{99m}Tc-DTPA, ^{99m}Tc-DMSA, ^{99m}Tc-HIDA, ^{99m}Tc-MDP, ^{99m}Tc-Pertechnetate (for thyroid imaging) and ^{18}F-FDG (whole body imaging), ^{99m}Tc-Sestamibi cardiac scan (rest and stress) 2-day protocols, ^{99m}Tc-parathyroid and ^{99m}Tc-labeled GI bleeding. The pediatrics were divided into three age groups of (> 1–5), (> 5–10) and (> 10–15) years. The observations show that, in most of cases, children are administered higher quantities of radiopharmaceuticals than recommended by guidelines. However, the adults are given right amount of does in most of the imaging procedures. It is shown that findings of the study can enable facilities to compare their radiation doses to the international guidelines and adjust them according to patient body size and weight to get image quality corresponding to right radiation dose.

Keywords: diagnostic reference levels / achievable doses / administered radioactivities / radiopharmaceuticals / optimization / nuclear medicine

1 Introduction

Nuclear medicine is the study of the applications of ionizing radiations for diagnosis and treatment of diseases. Different imaging procedures, whether nuclear medicine scans and those in diagnostic radiology, using ionizing radiation carry some level of detrimental effect. This is also evident by the linear no-threshold theory which correlates the induction of cancer to the amount of dose absorbed. Contrary to past, the role of nuclear medicine and radiation protection is increasing with advancing complexities in technology and treatment delivery. Better image quality has always been a priority of the interpreting physicians which can only be achieved at large amount of radiation doses. However, this high dose increases the probability of damage the tissues and can cause the cancer problems. In past, the patient dose limits were not existed; however, different efforts were being made around the globe to optimize the radiation exposure. For the concept of diagnostic reference levels (DRLs) was introduced to manage the current practices and to develop the ways to reduce the radiation exposure, whenever it is undue the DRLs. The DRLs and achievable doses (ADs) are becoming increasingly consistent tools for hospitals to manage their patient radiation doses. Traditionally, the DRLs have been applied in computed tomography; anyhow they have now been extended to interventional radiology, mammography, general x-ray, NM and even to dental X-ray (Bailey *et al.*, 2014).

The concept of reference levels in diagnostic imaging using ionizing radiation got attention when a considerable variation in radiation dose delivered to patients was found even for the same imaging exam during a survey of X-ray examinations in 1950 in Europe. Similarly, in United States, the concept of these reference levels originated after the "Nationwide Evaluation of X-ray Trends" survey in 1975–1981 (Alessio *et al.*, 2015). Realizing the potential detrimental effects of ionizing radiations, a number of researchers addressed this issue in their publications (see end) and defined these reference levels. Therefore, a considerable variation exited in the definition of these levels, however, two of them gained a widely accepted recognition: one is diagnostic reference levels (DRLs) and the other is Achievable Doses (ADs). The goal of establishing these reference levels was to

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achieve optimization in medical exposure of patient for the purpose of diagnosis. It implies that exposure of radiation must be commensurate with the image of diagnostic quality; neither low nor higher than that.

For optimization of patient imaging as well as radiation protection, the DRLs are considered as standard were first made public by the International Commission on Radiological Protection (ICRP) in 1990 (ACR–AAPM, 2015) and then explained more in detail in 1996 (Lassmann *et al.*, 2008). The ICRP report identifies two main points for machine; one is validation and other most effectiveness of radiology assessments. The validation means that the assessment is shown and the patient's takes additional any possible disadvantages. Effectiveness means that the radiation exposure is most effective use for the clinical point of the assessment. The dosage is achievable by adopting standard strategies while keeping up clinical picture quality sufficient for analytical reasons (NCRP, 2012). After establishing the importance of these reference levels, many countries have established their own reference levels in diagnostic radiology and nuclear medicine based on the local clinical practice (JIRA, 2015: EC, 2014). National Council on Radiation Protection and Measurements (NCRP report no. 172) proposed reference levels in nuclear medicine in children through surveying of 13 leading hospital in US (NCRP, 2012; Gelfand *et al.*, 2011). Later, these were also published by American College of Radiology (ACR) (ACR–AAPM, 2015). Similarly European Association of Nuclear Medicine (EANM) dose card has been published based on recommendations by Pediatric Task Group EANM in Europe (Lassmann *et al.*, 2008). These dose cards provide guidelines of administering radioactivity to patients for a variety of ages and weights. Furthermore, a harmonization between these American and European guidelines was also developed in order to remove any discrepancy existed between the guidelines (Lassmann and Treves, 2014).

DRLs and AD for adults are usually characterized for a "standard patients or standard phantoms". For pediatric, there is no such solitary term exist because of vast size scope of pediatrics. Some authors recommended a practical approach of utilizing four age bands of < 1 y, > 1–5 y, > 5–10 y, and > 10–15 years (Vassileva and Rehani, 2015). Instead of age, weight band is a more practical approach to set reference levels due to poor correlation between age and weight. Other than these two parameters, children body surface area can also be used for this purpose. Nonetheless, if latter parameters are not available, age alone may be used to establish these reference levels.

Contrary to diagnostic radiology, the calculation of organ doses in nuclear medicine is not straightforward and varies from patient to patient due to individual specific biokinetics of the patient (Valentin, 2004). Therefore, radiation dose metrics, that are used to establish DRLs and AD in diagnostic radiology, cannot be implemented exactly in nuclear imaging. Instead, the easily measured quantities in nuclear medicine are administered activities (measured in MBq). However, the amount of isotope injected is a function of weight and age of the patient as well as the type of clinical investigation and sensitivity of the instrument. Small patients should be given limited amount of radiopharmaceuticals as opposed to adults that require higher amount of radiation doses. Mean effective dose in most nuclear exam is from (0.3–20) mSv (Gelfand *et al.*, 2011).

Due to the lack of knowledge of current practice of administering activities as well as reference levels, the quantity of radioactivities given to pediatrics and adults patients was determined through survey of facilities performing them. The reference levels will then be determined based on the results of collected data and will be disseminated to the participating institutions. To the best of our knowledge, no such previous work has been performed country wide so far. Therefore, there is a dire need of establishing reference levels to optimize the radiation exposure to patient populations. It is expected that these reference levels will be adopted by hospitals in their routine practice for optimization of medical exposure to patients. The study was carried out in PINUM Cancer Hospital Faisalabad Pakistan.

2 Material and methods

A survey was conducted for general nuclear medicine, nuclear cardiac and PET procedures to get data of administered activities given to patients of varying ages. The data was collected from Govt. as well as from private hospitals practicing imaging procedures using ionizing radiation. The cohort of patients included adult and pediatric both male and female. The survey forms were sent to medical physics departments of the participating institutions and medical physicists filled the survey data forms manually. It was observed that only a few of the facilities performed all types of imaging scans; however, some of them were dedicated cardiac centers. Currently, most of the participating institutions measure radioactivity in the units of mCi, however, in the current research work and for the sake of comparison with international guidelines, the radioactivities were expressed in the units of MBq. For imaging facilities performing all types of exams, only those nuclear medicine procedures were included in the surveys that were commonly performed to get sufficient data. The commonly performed imaging procedures in children were ^{99m}Tc-DTPA, ^{99m}Tc-DMSA, ^{99m}Tc-HIDA, ^{99m}Tc-MDP, ^{99m}Tc-pertechnetate (for thyroid imaging) and ^{18}F-FDG. In adults, other than these, ^{99m}Tc-sestamibi (rest and stress), ^{99m}Tc-parathyroid and ^{99m}Tc-labeled RBC (for GI bleeding) were also performed (Table 1). Although PET is the fastest growing study type in nuclear medicine (NCRP, 2012) around the world, limited data is available due to infrequent PET scanners as compared to general nuclear medicine scans. Furthermore, current the almost all facilities performed whole body PET studies.

For each exam, number of patients, age, minimum and maximum amount of radioactivity administered were asked. To get good counting statistics and to make sure that the data will be of truly representative of the current practices, an attempt was made to include as many patients as possible. A data of about 2020 patients was gathered. Out of 2020, 1138 were adults (male or female) and 882 were children of varying ages. Approximately, 75% of NM centers participated in this survey while 25% of the selected institutes did not respond to this study. Only two medical centers participated in this survey have PET/CT along with cyclotron facility. One hospital is a pure cardiac center and therefore performs only cardiac tests using Tc-99m radioisotope. We adopted 75th and 50th

Table 1. Names of routine nuclear medicine procedures used in the survey for data collection.

Tc-99m pertechnetate (for thyroid imaging)	Tc-99m diethylenetriamine pentaacetic acid (DTPA) renal scan	Tc-99m dimercaptosuccinic acid (DMSA)
Tc-99m parathyroid	Tc-99m hepatobiliary iminodiacetic acid (HIDA) scan	Tc-99m methyl diphosphonate (MDP)-bone scan
Tc-99m methoxy iso butyl isonitrile (MIBI) stress (2-day protocol)	Tc-99m methoxy iso butyl isonitrile (MIBI) rest (2-day protocol)	F-18fluorodeoxyglucose FDG (whole body PET scan)

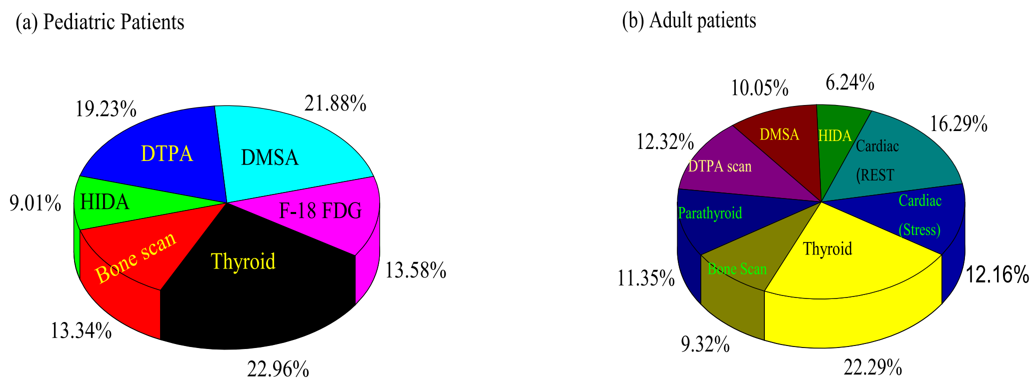

Fig. 1. Distribution of number of imaging scans among pediatrics and adults patients. Comparison of imaging scans with present (a) five pediatric scans of: thyroid, bone, HIDA, DTPA, and DMSA, and (b) eight adult scans: thyroid, bone, parathyroid, HIDA, DTPA, DMSA, cardiac rest and cardiac stress, respectively. It can be seen that thyroid scans are frequently performed scans; however, HIDA scans are rare NM procedures among adults and pediatrics.

percentiles values of the facilities distribution of administered activities as recommended level for DRL and AD. The reference values were then compared with those of other countries.

3 Results and discussion

Figure 1 shows the distribution of different imaging scans among adults (male and female) and pediatric patients. For both cases, data regarding NM imaging scans were collected with setting of eight scans for adults and five scans for pediatrics along with different number of patients from various hospitals. It is shown from figure that the thyroid scan was 22.96% of the total pediatric procedures thereby ranked the most commonly performed procedure in children. However, cardiac scan was most frequently performed test among adults being 28.45% (both rest and stress) of total scans. It was to be noted that the Tc-99m HIDA scan was rare both in children's and adults with 9.01 and 6.24% among children and adults, respectively. It was observed that DMSA (25%) and DTPA (22%) scans, for pediatric patients, were also frequent NM procedures, however, DMSA (10.05%) and DTPA (12.32%) scans were comparatively rare NM scans in case of adults patients. It was further examined that the moderately performed scans were bone scan 13.34% (10%) for pediatric (adults) patients. It can be seen from Figure 1 that the F-1 FDG (13.58%) and parathyroid (11.35%) scans were observed for pediatric and adult patients. During the collection of data, it was observed that majority of local hospitals adopt age of the patient and not the weight, as it was determining factor in finding administered activates although a few were using weight for this purpose. The international guidelines recommend activities based either on the weight or body surface area of the patients, this condition, however, can be relaxed in situations where weight based data is not available. In order to compare the range of administered activities with the international guidelines, weight distribution of patients were determined for the age groups of (> 1–5), (> 5–10) and (> 10–15) years. The corresponding average weights were 12.94 ± 1.56 kg, 24.08 ± 3.84 kg and 40.66 ± 8.06 kg respectively (Mushtaq *et al.*, 2012). It must be taken into account that this distribution of weight does not a truly representative of pediatric patient population weight during visiting hospital due to very small sample size. The adult patient weight was assumed to be 70 ± 10 kg. It was surprising to note that higher activities were prescribed depending upon the local clinical practice for markedly obese patients and it was varied among various hospitals. It was examined that one hospital was using 350 MBq for F-18 FDG whole body imaging for adults of 70 kg using 5 MBq/Kg and it was further raised these activities for obese patients with a maximum of 450 MBq.

We studied the accuracy and consistency of the administered activities, the administered activities were further compared with those recommended by Society of Nuclear Medicine and Molecular Imaging (SNMMI) (SNMMI, 2018)

Table 2. 75th and 50th percentile values for pediatric of age group (> 1–5) years. Minimum and maximum values are also compared with those of SNMMI and EANM values.

Exam	Pat No.	Min (MBq)	Max (MBq)	DRLs (75th percentile)	AD (50th percentile)	UK EANM (EANM, 2008)		USA SNMMI[a] (MBq) (SNMMI, 2018)
						Min. (MBq)	Max. (MBq)	
Tc-99m pertechnetate (for thyroid imaging)	37	37	74	67	52	10	20	16
Tc-99m DTPA	63	37	106	96	76	24	62	–
Tc-99m HIDA	75	74	148	136	105	20	47	19
Tc-99m DMSA	61	111	185	164	142	18	30	19
F-18 FDG (whole body)	32	70	95	82	79	24	62	22

[a] Minimum activity based on the minimum weight of the distribution of weights of that age group.

Table 3. 75th and 50th percentile values for pediatric of age group (> 5–10) years. Minimum and maximum values are also compared with those of SNMMI and EANM values.

Exam	Pat No.	Min	Max	DRLs (75th percentile)	AD (50th percentile)	UK EANM (EANM, 2008) Min. (MBq)	Max. (MBq)	USA SNMMI[a] (SNMMI, 2018)
Tc-99m pertechnetate (for thyroid imaging)	81	74	111	99	79	27	38	23
Tc-99m MDP	51	296	370	355	324	170	240	194
Tc-99m DTPA	45	70	168	129	95	68	96	–
Tc-99m DMSA	77	148	185	177	156	33	47	39
F-18 FDG (whole body)	38	85	105	97	89	68	96	78

[a] Minimum activity based on the minimum weight of the distribution of weights of corresponding age group.

and European Association of Nuclear Medicine (EANM) dose card (EANM, 2008). The EANM (2014) administered activity was determined by the following formula.

$$A[MBq]_{ad\ ministered} = baseline\ \ Activity \times Multiples, \quad (1)$$

where multiples of baseline activities depend on the type of class of radiopharmaceuticals. To determine the reference activities for comparison using the above formula, the weight distribution was mentioned in Ref. (Lassmann *et al.*, 2008).

The administered activities (AAs) situation is shown in Tables 2–4, where we recorded the main results of our survey that indicated a variation in administered activities among different institutions in most of nuclear medicine studies. These tables show minimum and maximum administered activities along with 75th and 50th percentile values of calculated administered activities for five different NM scans of Tc-99m Pertechnetate (for thyroid imaging), Tc-99m DTPA, Tc-99m HIDA, Tc-99m DMSA and F-18 FDG (whole body) with different number of patients. These tables also present the recommended results taken from EANM (EANM, 2008) and SNMMI (SNMMI, 2018) at nearly the same number of patients, for comparison with our own results and three age groups of (> 1–5), (> 5–10), and (> 10–15) years. Here, we first discuss the AAs illustrated in Table 2 for number of patents of 37, 63, 75, 61 and 32 corresponding to above mention five different NM scans. It was noted that the obtained maximum and minimum administered activities were significantly higher than that of earlier recommended values of EANM (EANM, 2008) dose card and SNMMI results (SNMMI, 2018), for five major scans of age group (> 1–5) years. It was shown that the AD (50th percentile) values of Tc-99m DTPA and F-18 FDG (whole body) were in close agreement with earlier maximum recommended EANM results (EANM, 2008). However, a significant difference came upon especially for Tc-99m DMSA scan where the minimum activity was 111 MBq contrary to 18 MBq (or 19 MBq) of recommended EANM values (EANM, 2008). Similar trends were observed in Table 3 and it can be seen that the minimum and maximum activities of age group (> 5–10) except for Tc-99m DTPA where the minimum activity of 70 MBq approaches to EANM recommended value of 68 MBq. However, the maximum activity (168 MBq) of Tc-99m

Table 4. 75th and 50th percentile values for pediatric for age group (> 10–15) years. Minimum and maximum values are also compared with those of SNMMI and EANM values.

Exam	Pat No.	Min (MBq)	Max (MBq)	DRLs (75th percentile)	AD (50th percentile)	UK EANM (EANM, 2008)		USA SNMMI (SNMMI, 2018)
						Min. (MBq)	Max. (MBq)	
Tc-99m pertechnetate (for thyroid imaging)	73	74	185	177	130	43	56	43
Tc-99m MDP	60	592	740	690	642	270	350	361
Tc-99m DMSA	45	95	210	198	179	52	68	72
Tc-99m DTPA	52	111	155	152	132	108	140	–
F-18 FDG (whole body)	43	85	110	102	97	108	134	144

Table 5. 75th and 50th percentile values for adults (> 18 years). Minimum and maximum values are also compared with those of SNMMI minimum and maximum values.

Exam	Pat No.	Min (MBq)	Max (MBq)	DRLs (75th percentile)	AD (50th percentile)	USA SNMMI (SNMMI, 2018)	
						Min. (MBq)	Max. (MBq)
Tc-99m pertechnetate (for thyroid imaging)	275	148	200	188	163	74	370
Tc-99m MDP	115	555	944	886	650	740	1110
Tc-99m parathyroid	140	666	740	715	690	–	–
Tc-99m GI bleeding	52	495	925	877	725	555	1100
Tc-99m DTPA	152	74	370	325	195	37	1110
Tc-99m sestamibi (rest)	201	298	815	755	604	740	1480
Tc-99m Sestamibi (Stress)	150	264	1258	984	710	740	1480
F-18 FDG (whole body)	53	350[a]	450	358	320	370	740

[a] Assuming 5 MBq/Kg for adults upto a maximum of 450 MBq for obese patients.

DTPA was definitely higher as compared to previously EANM recommended value (96 MBq). It can be seen that the maximum activity (105 MBq) of F-18 FDG (whole body), for age group (> 5–10), agreed well with maximum value (96 MBq) of EANM. It was interesting to note that AD (50th percentile) values of Tc-99m DTPA and DRL (75th percentile) of F-18 FDG (whole body) were in reasonable agreement with maximum recommended EANM data (EANM, 2008). For children of age group (> 10–15) years, the minimum activity Tc-99m DTPA is 111 MBq which is close to the recommended values, however, the F-18 FDG activity is 85 MBq which is less than the minimum activities of 108 and 144 MBq as suggested by EANM and SNMMI respectively (Table 4). It is concluded from Tables 3 and 4 that a significant difference was noted for Tc-99m DMSA scan where the minimum and maximum activities were 148 MBq (95 MBq) and 185 MBq (210 MBq) respectively contrary to 33 MBq (52 MBq) and 47 MBq (68 MBq) of recommended EANM values, for age group of > 5–10 years (for age group of > 10–15). The selection of appropriate administered activity depends on a number of parameters, however, for children, local clinicians use higher activities for children for faster acquisition of study.

Table 5 displays the minimum and maximum values of AAs for eight different NM scans of Tc-99m pertechnetate (for thyroid imaging), Tc-99m MDP, Tc-99m parathyroid, Tc-99m GI bleeding, Tc-99m DTPA, Tc-99m sestamibi (Rest), Tc-99m sestamibi (Stress) and F-18 FDG (whole body) with number of patents of 275, 115, 140, 52, 152, 201, 150 and 53, respectively, for adults. It is significant to note that our results of maximum and minimum AAs were lower as compared to the earlier results reported by SNMMI, for seven NM scans. It can be seen from Table 5 that the minimum value of AAs, for Tc-99m pertechnetate thyroid imaging (148MBq) and Tc-99m DTPA (74 MBq), is significantly higher than but for Tc-99m GI bleeding (495MBq) and F-18 FDG whole body (350 MBq) lie close to the earlier recommend SNMMI dose values. For adults, the other minimum activities for Tc-99m MDP bone scan (555 MBq), Tc-99m sestamibi rest (298 MBq) and Tc-99m sestamibi stress (264 MBq) were lower than the SNMMI recommended values. It is examined that the large differences in maximum activity could be seen in Tc-99m GI bleeding where the recommended value differed by an amount of 740 MBq. Other notable differences in maximum values were for Tc-99m sestamibi (rest) and F-18 FDG.

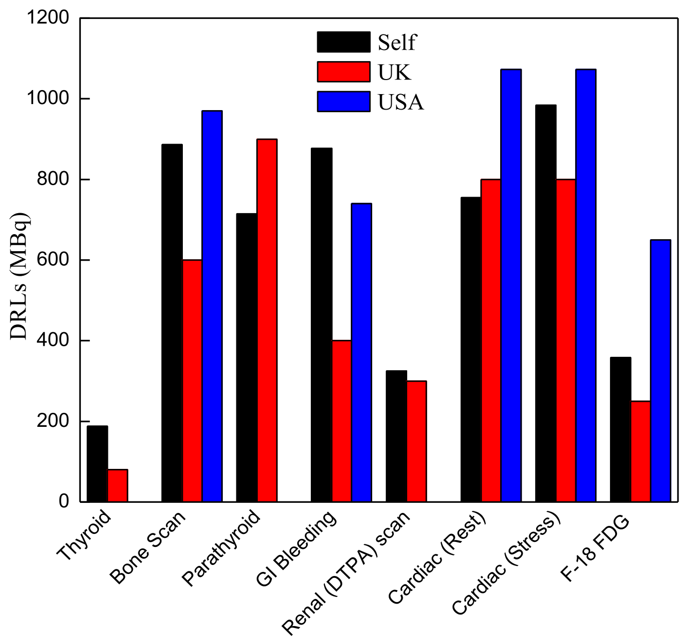

Fig. 2. Comparison of present DRLs of adults with those of US SNMMI (SNMMI, 2018) and ARSAC-UK (ARSAC, 2000) DRLs, for eight (thyroid, bone, parathyroid, HIDA, DTPA, DMSA, cardiac rest and cardiac stress) mentioned NM scans. All scans, except PET scan were done with Tc-99m radioisotope.

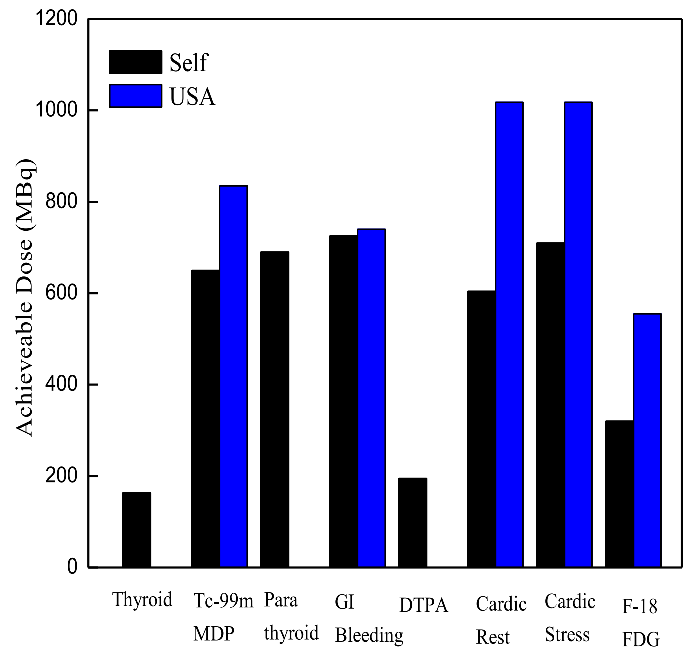

Fig. 3. Comparison of present ADs of adults with those of US SNMMI reference values (SNMMI, 2018), for eight (thyroid, bone, parathyroid, HIDA, DTPA, DMSA, cardiac rest and cardiac stress) mentioned NM scans.

Moreover, the 75th (for DRLs) percentile and 50th (for ADs) percentile of the NM scans were also calculated for pediatrics of all age groups as well as for adults (Tables 2–5). It should be pointed out here that reference levels determined did not correspond to the nuclear medicine practice on national level, notwithstanding, these were based on the best data available we have for nuclear medicine modalities. It is noted that the administered activities to children of age group (> 15–17) years have not been included in this study due to limited data available. Therefore the comparison was made only for those scans for which the reference values were available.

Figures 2–5 show the DRLs and ADs for adults and children's for various NM scans as well as the DRL values provided by ARSAC (administration of radiopharmaceutical and use of sealed radioactive source) committee for UK population (ARSAC, 2000) and USA (SNMMI, 2018). It was observed from Fig. 2 that the DRLs for thyroid, bone, GI bleeding, 2-day cardiac (stress) and F-18 FDG whole body imaging were higher than the reference values provided by ARSAC-UK population (ARSAC, 2000), however, the DRLs for parathyroid, renal (DTPA), cardiac (rest) were found lower. The US DRLs exceeded in most of the cases except for Tc-99m GI bleeding where it was lower than our value by 133 MBq (ACR–AAPM, 2015). It is to be noted that the DRLs of ARSAC-UK lie between US DRLs and our own values for bone, GI bleeding, cardiac (rest), cardiac (stress) and F-18 FDG scans. Furthermore, Fig. 3 demonstrates the ADs as a function of different NM scans along with US DRLs (ACR–AAPM, 2015) and it can be seen that the US recommended ADs were significantly higher than those obtained from survey of clinical facilities for Tc-99m MDP, Tc-99m Sestamibi cardiac rest and stress and F-18 FDG scans. In case of Tc-99m GI bleeding, our ADs results are in practically good agreement with earlier US data.

Figures 4 and 5 show that the DRLs and ADs for children of three age groups. The US DRLS and ADs values exceeded our reference values determined through surveyed in case of Tc-99m MDP and F-18 FDG scans. However, for Tc-99m DMSA, the local DRLs are less than those of US DRLs. The reference values of DRL for Tc-99m DTPA and Tc-99m thyroid scans are not available; therefore, we only included our own values in the corresponding figures. Similar trend was found in case of achievable doses (ADs). It should be noted that the low values of reference levels do not reflect poor practices of the hospitals.

3.1 Limitation

The study did not include all the hospitals practicing nuclear medicine. Furthermore, it did not include imaging procedures that are not commonly performed. There is also a need to include large number of patients especially from pediatric population to have an accurate assessment of reference levels.

4 Conclusions

The diagnostic reference levels (DRLs) and achievable doses (ADs) are considered as important tools to optimize patient radiation exposure without compromising image quality. These levels are established, for nuclear medicine

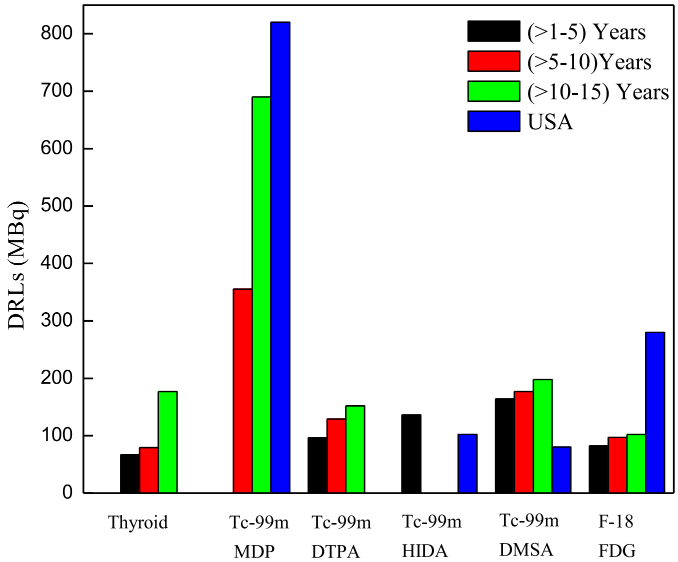

Fig. 4. Comparison of present DRLs of children with those of US SNMMI DRLs (SNMMI, 2018), for six (thyroid, Tc-99m MDP, Tc-99m DTPA, Tc-99m HIDA, Tc-99m DMSA and F-18 FDG) NM scans with three age groups of (> 1–5), (> 5–10) and (> 10–15) years. The diagnostic reference values for Tc-99m DTPA and Tc-99m thyroid scans are not available.

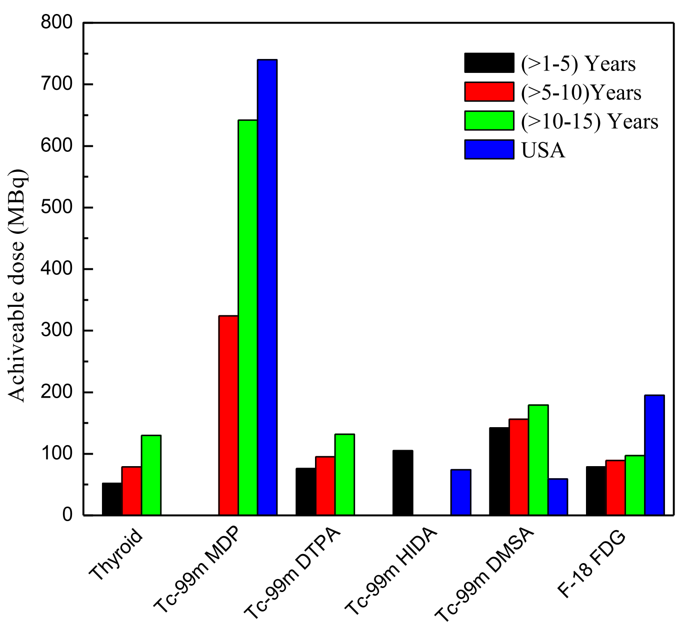

Fig. 5. Comparison of present ADs of children with those of US SNMMI DRLs (SNMMI, 2018**)**, for six (thyroid, Tc-99m MDP, Tc-99m DTPA, Tc-99m HIDA, Tc-99m DMSA and F-18 FDG) NM scans with three age groups of (> 1–5), (> 5–10) and (> 10–15) years. The diagnostic reference value for Tc-99m DTPA and Tc-99m thyroid scans are not available.

imaging procedures, through a survey of local clinical practices of administering radiopharmaceuticals. These reference levels are utilized to achieve a balance between radiation dose and diagnostic accuracy of the patient images. The reference values are normally set at 75th and 50th percentile values for DRLs and ADs respectively. Activities based on patient body weight or body area provide an accurate estimation of the right amount of radiopharmaceuticals to be injected for the right clinical examination and for right diagnosis. However, age based administered activities and thus reference levels can also be used when weight based data are not available. Deviations from these reference levels should have to be expected but such shift should be investigated thoroughly to determine the cause and adopt strategies to avoid such reoccurrence in future.

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Cite this article as: Shahzad A, Bashir S, Anwar A. 2019. Establishment of age-specific reference levels and achievable doses for children and adults undergoing nuclear medicine exams. *Radioprotection* 54(3): 187–194