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Research Article

Relative renal functions for children using ^{99m}TC-DTPA and ^{99m}TC-DMSA

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ABSTRACT

Radionuclides are widely used to study the relative renal functions (RRFs) for kidney patients. This work reports the determination of the RRFs using the technetium-99m dimercaptosuccinic acid (^{99m}Tc-DMSA) and technetium- 99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) for children having kidney diseases. The two methods are then compared to find the choice of scintigraphy for a particular type of disease. A total of 65 child kidney patients of ages 5 months - 16 years were the representative samples of the study. The mean RRFs calculated with ^{99m}Tc-DTPA were found as 47.10%±19.81% and 53.33%±19.50% ,respectively, for the left and right kidneys. On the other hand, the values are 46.66%±20.02% and 53.31%±20.01%, respectively, using ^{99m}Tc-DMSA.A significant positive correlation (r=0.944,P<0.001) was found between the RRFs calculated with the two scanning methods in pearson correlation analysis. In one way ANOVA test, we did not find any difference between the RRFs calculated with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA between the left and right kidneys. In Bland-Altman Plots, no mean difference was found between the two scanning methods and the correlation limit lies between 13.5 and 12.6. The present study suggests using a single method for a particular type of disease.^{99m}Tc-DMSA is the primary choice for the evaluation of RRF since it is easy, inexpensive and also provides cortical morphology, renal scar and cyst evaluation. But for glomerular filtration rate and renogram curve, ^{99m}Tc-DTPA should be the obvious selection as 99mTc-DMSA fails to provide any information for these cases. fails to provide any information for these cases.

Introduction

Renal scintigraphy is an imaging method that uses a small amount of radioactive materials called radiopharmaceuticals, a gamma camera and a computer to evaluate the kidney functions and its anatomy. It determines whether the kidneys are working properly. It can provide distinctive information that is often unattainable using other imaging techniques. Relative renal function (RRF) has usually been measurements by radionuclide renal scintigra-

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phies using different tracers for a long time (Hackstein et al., 2007). These measurements can be performed by different radiopharmaceuticals such as technetium-99m-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA), technetium-99m-dimercaptosuccinic acid (^{99m}Tc-DMSA), technetium-99m-mercaptoacetyltriglycine (^{99m}Tc-MAG3), Iodine-131 orthoiodihippurate, and technetium-99m-ethylenedicysteine (^{99m}Tc-EC) (Moran 1999). All of them can be used to accurately measure the RRFs, although there are some differences among the RRFs calculated with these radiopharmaceuticals (Taylor and Lallone, 1985). The differences are due to the different distinct biological properties of radiopharmaceuticals such as the mechanism of renal excretion, renal cell retention of radioactive materials, level of plasma protein bound, and level of plasmatic clearance. The relative renal function (RRF) or split renal function (SRF) or differential renal function (DRF), expressed as a percent of total renal function (Dostbil et al., 2011), is very important for patients with unilateral renal disorders and is used to understand sufficient postoperative renal function. The evaluation of the RRF of each kidney, separately, is important in the initial assessment and treatment of patients with renal diseases.

^{99m}Tc-DMSA is a static renal scintigraphy, which is considered as the most reliable method to measure the RRFs (Ardela et al., 2002; Kawashima et al., 1998; Piepsz, 2002). It is regarded as the most appropriate tracer for renal cortical imaging (Piepsz et al., 1999). DMSA renal scan shows the relative distribution of functional tissue and is primarily used in humans for cortical imaging and estimation of functional renal mass (Daniel et al., 1999; Müller-Suur and Gutsche, 1995; Campbell and Powers, 2003). Applications in humans also include the detection of pyelonephritis (Majd and Rushton, 1992) and renal scars (Hitzel et al., 2004; Shanon et al., 1992). On the other hand, ^{99m}Tc-DTPA dynamic renal agent, which is neither secreted nor resorbed by the kidney tubules, is freely filterable with the glomerulus. This method can measure total and individual functions as well as glomerular filtration rate (GFR) (Itoh, 2011; Momin et al., 2018). There are limited works for the calculation of the RRFs using ^{99m}Tc-DTPA and ^{99m}Tc-DMSA in adults and children. Recently, Momin et al. (2018) calculated the RRFs for patients of wide age ranges using ^{99m}Tc-DTPA and ^{99m}Tc-DMSA. In their study, they suggested using ^{99m}Tc-DMSA for the calculation of RRFs for cortical morphology and renal scar as it is an easy and inexpensive method (Nimmo et al., 1987). They also recommend the use of ^{99m}Tc-DTPA for glomerular function and renogram curve. In their work, Arteaga et al. (2017), using three radiopharmaceuticals ^{99m}Tc-DTPA, ^{99m}Tc-MAG3 and ^{99m}Tc-DMSA, found the lowest absorbed dose for ^{99m}Tc-MAG3 and highest for ^{99m}Tc-DMSA for newborns and 1-year old children. Çelik et al. (2014) performed renal studies for children using ^{99m}Tc-DTPA and ^{99m}Tc-DMSA, and found a good correlation (r = 0.963, P< 0.001) between the two methods.

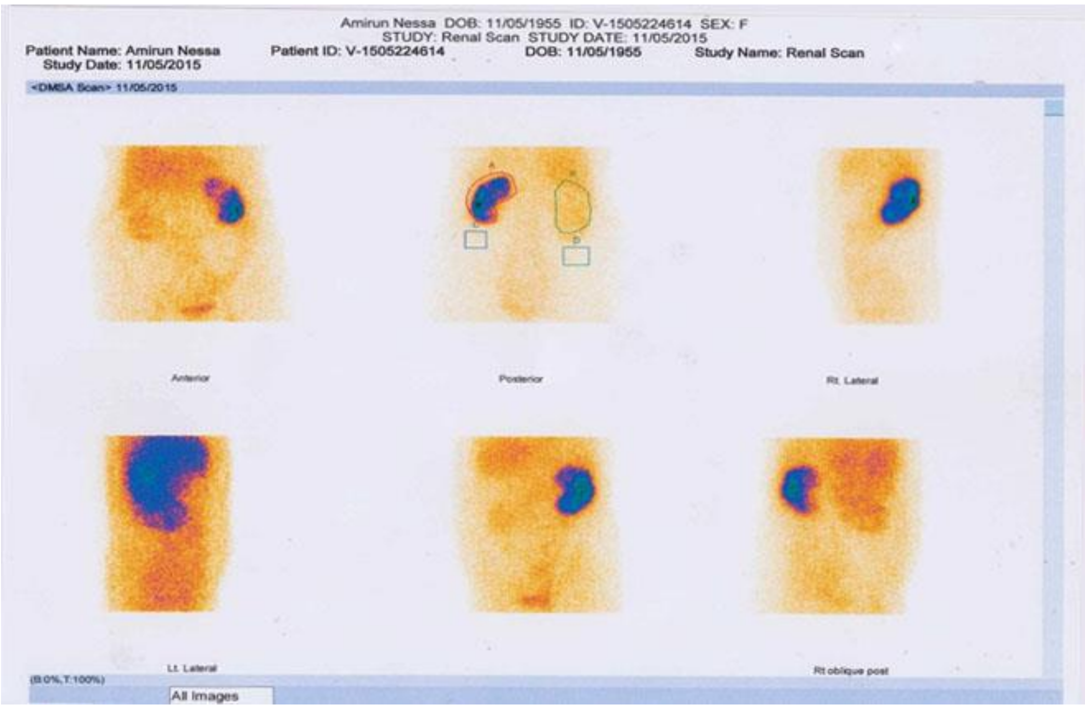
Domingues et al. (2006) compared the RRFs calculated with either ^{99m}Tc-DTPA or ^{99m}Tc-EC dynamic scintigraphy to those calculated with ^{99m}Tc-DMSA static scintigraphy for kidney patients of ages between 0.17 and 65 years. Their studies revealed that the RRFs measured with ^{99m}Tc-DTPA was almost identical to that measured with ^{99m}Tc-EC, but was significantly different from that measured using ^{99m}Tc-DTPA with a borderline statistical significance (P = 0.05). In the work of Itoh et al. (2011), a good correlation was found ($r = 0.992,\ P = 0.001$) between the relative renal uptake of ^{99m}Tc-DMSA and ^{99m}Tc-DTPA. But for GFR, the result is different with these two methods. Lee et al. (2010) compared the RRFs calculated with ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 form those calculated with ^{99m}Tc-DMSA for 18 rabbits. They found a good correlation ($p < 0.05$) and suggested that DTPA and MAG3 may be used in place of DMSA to measure the RRF. In 2012, ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 renal scintigraphies were compared for 57 patients by Bedriye et al. (2012) in terms of differential renal function based on ^{99m}Tc-DMSA renal scans. Their studies also gave similar results for RRFs measured with DTPA and MAG3 with those measured with DMSA.

Although there are some reports found in the literature for comparing the RRFs calculated with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA, (Nimmo et al., 1987; Hitzel et al., 2004; Domingues et al., 2006; Lee et al., 2010; Bedriye et al., 2012; Çelik et al., 2014; Arteaga et al., 2017; Momin et al., 2018) very few studies are done to calculate the RRFs for a particular age group of kidney patients. This study aims to calculate the RRFs with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA for children with renal diseases and then compare the two renal scintigraphies with one another. Section 2, in this paper, describes the materials and methods of the whole work. Section 3 presents an analysis of the study and obtained results. Section 4 is dedicated to the discussion, and concluding remarks are drawn in section 5.

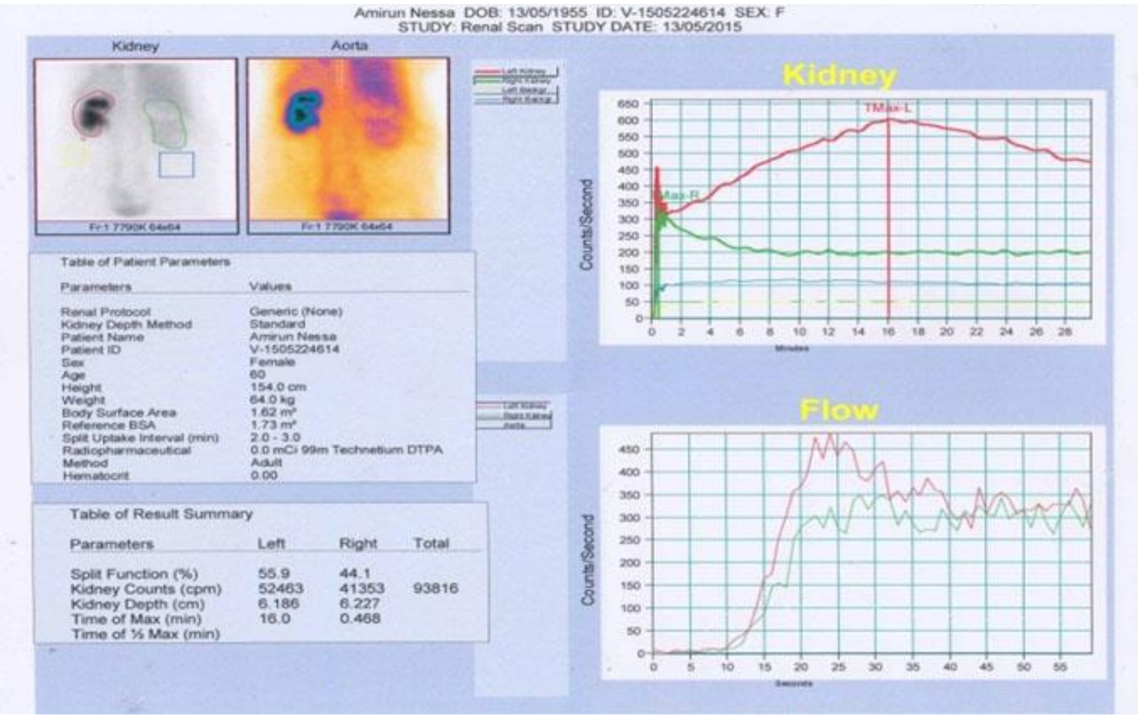
Materials and Methods

The representative samples of this study are 65 children, including 37 male and 28 female having age ranging from 5 months to 16 years who were referred from July 2018 to February 2019 to the Institute of Nuclear Medicine and Allied Sciences (INMAS) at Dhaka Medical College Hospital, Bangladesh, for the evaluation of the RRFs. In this study, the kidney images of all patients were taken by a gamma camera. Both the ^{99m}Tc-DTPA dynamic and ^{99m}Tc-DMSA static renal scintigraphies were performed for all the patients. In the supine position, ^{99m}Tc-DMSA static images were acquired for all patients. For this purpose, a dual head gamma camera equipped with all-purpose, low energy, and parallel-hole collimator was used. All patients were injected with 20 MBq–111 MBq (0.5 mCi–4.5 mCi) of the radiopharmaceutical and static images were acquired in 256×256 matrix after four hours in left and right posterior and then with oblique projections of both posteriors.

The background correction method was employed to calculate the kidney counts for both static ^{99m}Tc-DMSA and dynamic ^{99m}Tc-DTPA renal scintigraphy. At first, the renal



(a)



(b)

Fig. 1. Kidney image of a patient using (a) ^{99m}Tc-DMSA, (b) ^{99m}Tc-DTPA.

and semilunar background regions of interest (ROIs) were manually drawn which are shown in Fig.1. Then the kidney counts (photon counts) for DTPA and DMSA scans were noted from the images. In Figure 1, we have shown the typical images of a kidney patient using ^{99m}Tc-DMSA and ^{99m}Tc-DTPA. The RRFs were calculated from the counts using the following equation (Sinclair, 2003):

$$\text{Right kidney function (\%)} = \frac{\text{Right kidney counts} - \text{Background counts}}{(\text{right kidney counts} - \text{background counts}) + (\text{left kidney counts} - \text{Background counts}} \times 100\%.$$

The left kidney function has been found as

Left kidney function (%) = 100% – right kidney function (%).

Analysis and Results

Analysis was carried out for 65 child patients of ages ranging from 5 months to 16 years. The mean age of the patients is 5.84±4.27 years. The distribution of the patients by the type of diseases along with the range of patient's age and median for a particular type of disease is given in Table 1. Among the

Table 1. Distribution of the patients by type of diseases (*N*=65)

Type of disease	Frequency	Percentage (%)	Patient's age (year)	Median (year)
UTI	7	10.8	1 - 3.83	3.83
Abdominal pain	2	3.1	4 - 5	4.5
Fever and vomiting	1	1.5	2	-
HDN	2	3.1	9 - 11	10
Left sided HDN	21	32.3	2 - 16	7
Right sided HDN	11	16.9	0.5 - 13	6
Bilateral HDN	9	13.8	0.41 - 7	1.25
Bilateral mild HDN	2	3.1	3.5 - 14	8.75
Left sided mild HDN	4	6.2	5 - 15	7
Right sided mild HDN	2	3.1	0.12 - 6.25	3.19
Left sided gross HDN	4	6.2	0.75- 13.00	5.96
	N = 65	100	0.12- 15.00	

UTI: Urinary Tract Infection, HDN: Hydronephrosis.

Table 2. Results from the variance analysis (ANOVA test) for DTPA and DMSA

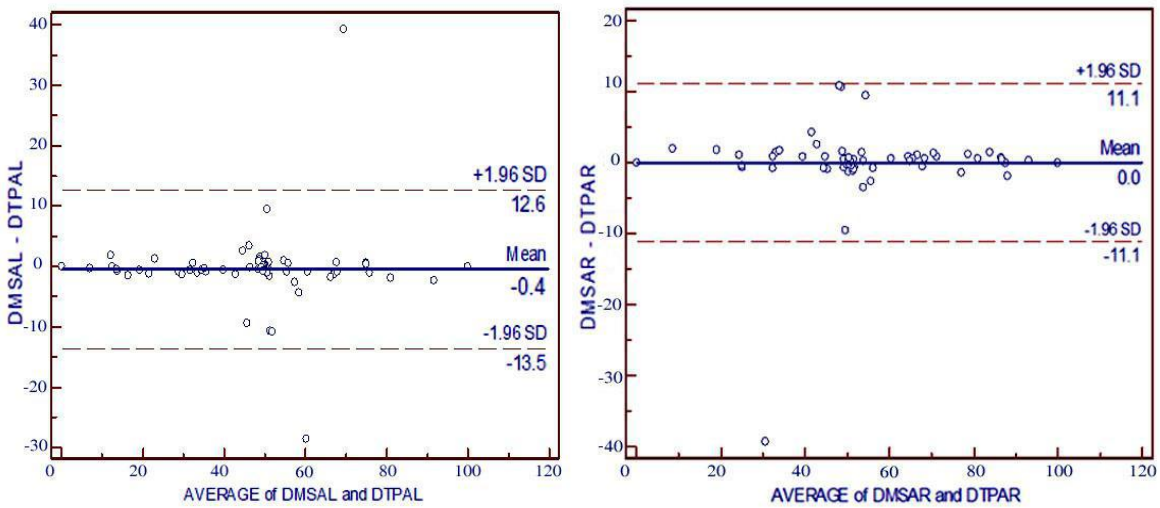
Disease type		DTPAL (%)	DMSAL (%)	DTPAR (%)	DMSAR (%)
UTI	Minimum	36.00	35.14	31.80	32.64
	Maximum	68.20	67.36	64.00	64.86
	Mean±SD	52.11±10.14	51.1±9.6	47.88±10.14	48.92±9.61
	Median	50.9	50.29	49.1	49.71
Abdominal pain	Minimum	.05	.05	49.50	49.76
	Maximum	50.50	50.24	99.95	99.95
	Mean±SD	50.45±35.67	25.1±35.5	74.72±35.67	74.85±35.48
	Median	25.28	25.1	74.72	74.85
Fever and vomiting	Minimum	50.90	50.57	49.10	49.43
	Maximum	50.90	50.57	49.10	49.43
	Mean±SD	50.90±0.0	50.57±0.0	49.10±0.0	49.43±0.0
	Median	-	-	-	-
Bilateral HDN	Minimum	48.0	48.70	18.10	10.90
	Maximum	81.9	89.10	52.00	51.42
	Mean±SD	56.8±12.2	61.3±15.2	43.21±12.24	38.96±15.38
	Median	49.9	58.09	50.9	49.7
Bilateral mild HDN	Minimum	49.3	49.10	49.47	48.80
	Maximum	50.5	51.20	50.70	50.90
	Mean±SD	49.9±0.87	51.2±1.48	49.91±.87	49.48±1.48
	Median	49.91	50.15	50.27	49.9
Left sided HDN	Minimum	12.40	12.40	41.40	44.00
	Maximum	58.60	56.00	87.60	87.60
	Mean±SD	36.3±12.7	36.3±13.3	63.75±12.73	63.55±13.35
	Median	35.5	34.6	64.95	65.4
Left sided mild HDN	Minimum	34.00	32.90	44.20	45.10
	Maximum	74.40	54.90	66.60	67.10
	Mean±SD	53.5±16.69	45.7±9.31	53.22±9.21	54.30±9.31
	Median	47.4	47.5	51.35	52.5
Left sided gross HDN	Minimum	7.20	6.80	86.00	86.80
	Maximum	14.00	13.20	92.80	93.20
	Mean±SD	11.5±3.14	11.5±3.15	88.50±3.14	88.47±3.15
	Median	12.4	13.5	87.6	86.95
Right sided HDN	Minimum	46.40	41.00	.00	.00
	Maximum	100.00	100.00	53.60	59.00
	Mean±SD	68.8±16.9	66.5±18.8	31.24±16.93	33.45±18.80
	Median	67.6	32.3	66.2	29.3
Right sided mild HDN	Minimum	54.30	46.00	43.00	50.51
	Maximum	56.70	55.20	45.70	52.07
	Mean±SD	55.5±1.69	50.60±6.50	44.50±1.69	49.40±6.50
	Median	55.5	44.5	50.6	49.4
HDN	Minimum	44.50	47.93	50.10	.00
	Maximum	49.90	49.49	55.50	99.95
	Mean±SD	47.2±3.81	48.71±1.10	52.80±3.81	51.29±1.10
	Median	47.2	48.71	52.8	51.29
Total	Minimum	0.05	0.05	0.00	0.00
	Maximum	100.00	100.00	99.95	99.95
	Mean±SD	47.10±19.81	46.66±20.02	53.33±19.50	53.31±20.01
	Median	49.90	46.00	52.07	50.59
***P*-value**		0.00	0.00	0.00	0.00

UTI: Urinary Tract Infection, HDN: Hydronephrosis.

patients, 10.8% had urinary tract infection (UTI), 3.1% have abdominal pain, 1.5% had fever and vomiting (FV), 3.1% had hydronephrosis (HDN), 32.3% had left sided HDN, 16.9% had right sided HDN, 13.8% had bilateral HDN, 3.1% had bilateral mild HDN, 6.2% had left sided mild HDN, 3.1% had right sided mild HDN, and 6.2% had left-sided gross HDN.

Pearson (bivariate) correlation analysis, using the software "statistical package for the social sciences (SPSS)" version 22, was performed for comparison of the RRFs calculated with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA renal scintigraphies for all the 65 patients. The mean, median, minimum (%), and maximum (%) values of RRFs, calculated for different types of renal diseases from the correlation analysis are presented in Table 2. The mean relative renal functions measured with ^{99m}Tc-DTPA was found 47.10%±19.81% and 53.33%±19.50%, respectively, for the left and right kidneys. With ^{99m}Tc-DMSA the values are, respectively, 46.66%±20.02% and 53.31±20.01%. The medians of the RRF are 49.90 and 52.07 for the left and right kidneys using ^{99m}Tc-DTPA. For ^{99m}Tc-DMSA the values are 46.00 and 50.59, respectively. The P-values was found $P = 0.0$ with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA for both kidneys.

The comparison of the results was expressed in Bland-Altman plots shown in Figures 2a and 2b. The mean difference between the two methods was 0.00, where the correlation limits lie between ˜13.5 and 12.6. The correlation analysis between the RRFs obtained from DTPA and DMSA for both kidneys are shown in Table 3. A significant positive correlation ($r = 0.994,\ P < 0.001$) was found between the RRF values calculated with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA. In one way ANOVA test, we have found $P = 0.00$ for both kidneys with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA. This means there is no difference foune between the calculated RRFs for the two kidneys. The results are graphically presented in Figures 3a and 3b.



(a) (b)

Fig. 2. Bland-Altman plots of DMSA and DTPA for the (a) left kidney and (b) right kidney.

Discussion

The measurement of the RRFs is one of the major contributions to the radionuclide renal studies in the practice of urology (Britlon et al., 1996). Both the dynamic DTPA and static DMSA are easy renal scintigraphies in the calculation of RRFs. According to Muller et al. (1995) and de Lange et al. (1989), ^{99m}Tc-DMSA gives the parenchymal function of the kidney visually and quantitatively and it is possible to calculate relative and absolute renal functions. In this work, both ^{99m}Tc-DMSA and ^{99m}Tc-DTPA scintigraphy was done by background correction methods by manually drawing the renal and semilunar background regions of interest (ROIs).

We also compared the RRFs calculated with ^{99m}Tc-DMSA and ^{99m}Tc-DTPA renal scans for 65 children of ages between 5 months and 16 years who had different kidney diseases. A positive correlation was found $(r = 0.994, P < 0.001)$ between the two calculations. The results of the present study agree well with the work of Momin et al. (2018), who found a positive correlation $(r = 0.997, p < 0.001)$ between the RRFs calculated with ^{99m}Tc-DTPA and ^{99m}Tc-DMSA. The results of the present study also agree with those of Campbell et al. (2003), Britlon et al. (1996) and de Lange et al. (1989) in which a good correlation was found between the renal uptakes of ^{99m}Tc- DTPA and that of ^{99m}Tc-DMSA. But the present study disagrees with the findings of Itoh (2011) and Domingues et al. (2006), according to whom the RRFs calculated with ^{99m}Tc-DTPA are different from those with ^{99m}Tc-DMSA with minimal statistical significance.

In the Bland-Altman plots shown in Figures 2a and 2b, the mean difference line is located very close to the zero lines. This shows a perfect agreement between the ^{99m}Tc-DTPA and ^{99m}Tc-DMSA in the calculation of the RRFs. Some values are out of range in Bland-Altman plots that correspond to the kidneys, which are atrophic or hydronephrotic (Çelik et al., 2014).

Table 3. Correlations between the relative renal functions calculated with ^{99m}Tc-DMSA and ^{99m}Tc-DTPA.

		DTPAL	DMSAL	DTPAR	DMSAR
DTPAL	P. Cor.	1	0.944**	-0.986**	-0.944**
	Sig. (2-tailed)		0.000	0.000	0.000
	N	65	65	65	65
DMAL	P. Cor.	0.944**	1	-0.959**	-1.000**
	Sig. (2-tailed)	0.000		0.000	0.000
	N	65	65	65	65
DTAR	P. Cor.	-0.986**	-0.959**	1	0.959**
	Sig. (2-tailed)	0.000	0.000		0.000
	N	65	65	65	65
DMAR	P. Cor.	-0.944**	-1.000**	0.959**	1
	Sig. (2-tailed)	0.000	0.000	0.000	
	N	65	65	65	65

P. Cor. - Pearson Correlation;**Correlation is significant at the 0.01 level (2-tailed).

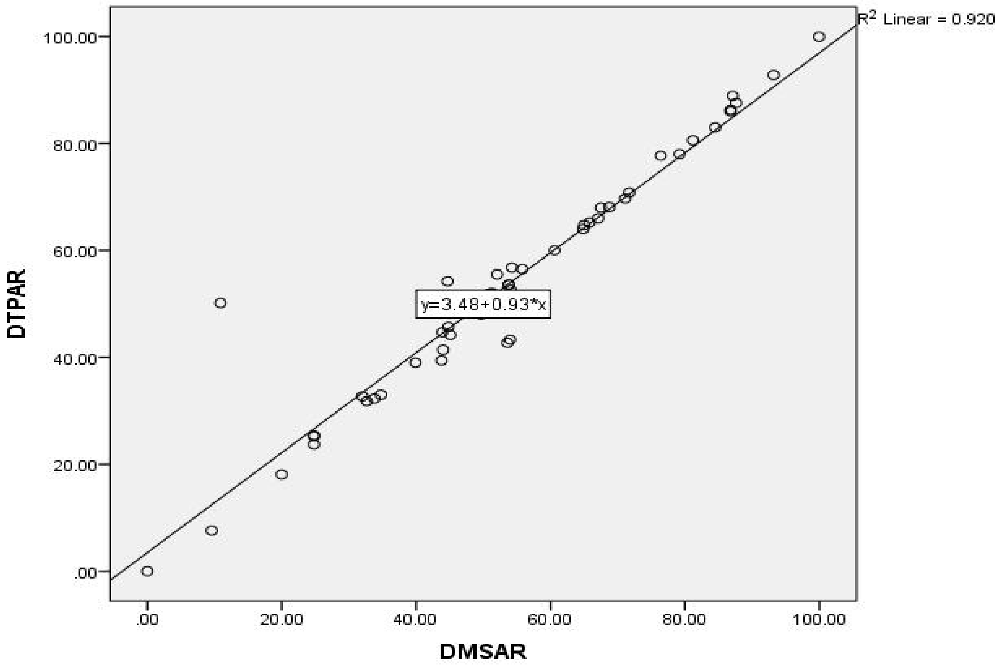


Fig. 3. Correlation between DTPA and DMSA for the left kidney.

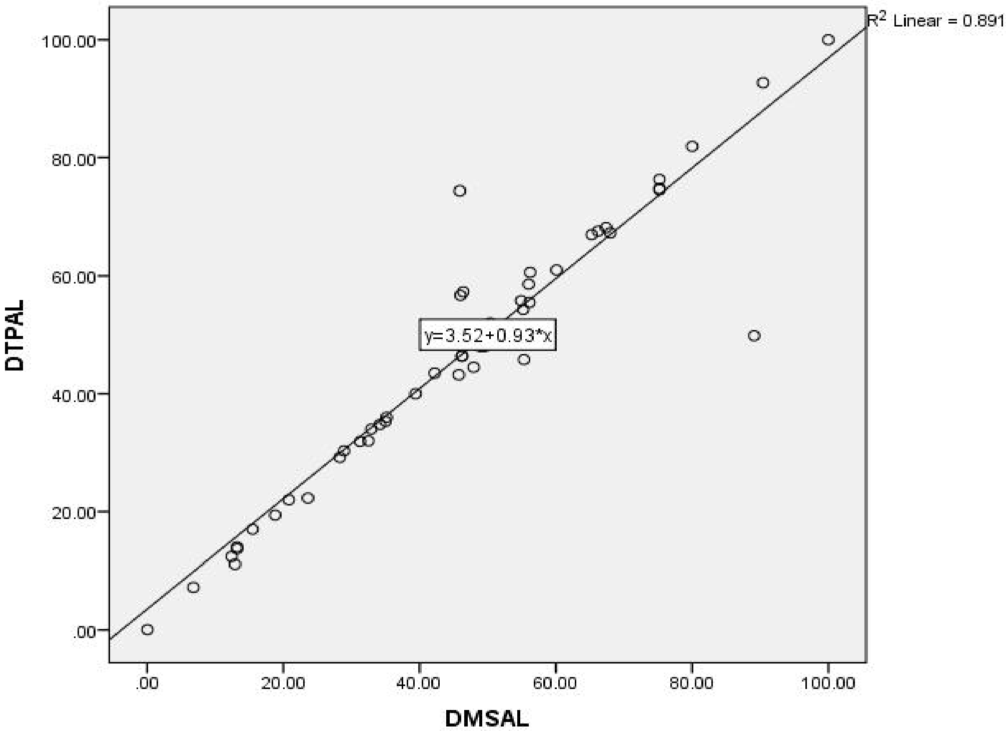


Fig. 4. Correlation between DTPA and DMSA for the right kidney.

Conclusions

The RRFs are calculated using the ^{99m}Tc-DTPA and ^{99m}Tc-DMSA scanning renal scintigraphies, and then compared with each other for both left and right kidneys of 65 patients. Both the scanning methods give almost similar results and are reliable in calculating the RRFs of kidney patients for pediatric age groups. ^{99m}Tc-DMSA is a static renal scintigraphy, which is an inexpensive and easy method, as it takes shorter times (Nimmo et al., 1987). But it fails to provide any functional information of the kidney.

As a result, we can conclude that ^{99m}Tc-DMSA should be the primary choice for calculating RRFs for cortical morphology and renal scar evaluation. But for glomerular filtration rate (GFR) and renogram curve, ^{99m}Tc-DTPA is the obvious selection.

For patients with renal diseases it is often advised to evaluate the renal functions with both ^{99m}Tc-DMSA and ^{99m}Tc-DTPA. But according to the results obtained from this work, any one of these two methods can be used for the calculation of RRFs depending on the type of kidney disease.

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