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Evaluation of MAG3 Renal Scan for Detection of Differential Renal Function and Renal Scar in Comparison to DMSA Scan in Pediatric Population

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Abstract: Chronic kidney disease (CKD) in children is a devastating illness with long-term effects. Globally the prevalence of CKD in childhood has been variously reported at 15 to 74.7 per million children with an increased burden in developing countries like Bangladesh. The aim of the study was to evaluate the efficacy of Tc-99m MAG3 renal scintigraphy for accurate measurement of DRF and detection of renal cortical scar in comparison to Tc-99m DMSA scan in the pediatric population. This cross-sectional observational study was carried out at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), BSMMU campus, Dhaka from July 2017 to June 2018. The study was conducted with ethical approval from Medical Research Ethics Committee (MREC). A total of 54 pediatric patients of different renal disorders were enrolled according to selection criteria and all patients underwent both Tc-99m MAG3 renal scintigraphy and Tc-99m DMSA scan by following the practiced protocol in NINMAS. A total of 54 pediatric patients (39 male and 15 female) with a mean age of 4.57 ± 4.40 years, ranging from 0.08 to 18 years had a mean height of 96.70 ± 31.70 cm and mean weight16.97±11.95 kg. The mean of DRF measured by DMSA and MAG3 was 54.22 ±20.38% and S1.47 ± 23.88% in left kidneys and 45.78 ± 20.38% and 48.51 ± 23.88% in right kidneys respectively. The Independent t-test showed the mean difference of DRF measured by two radiotracers was not statistically significant in both kidneys. There was a positive significant correlation between the two methods (Pearson correlation test, r-0.948, p-0.001 in the left kidney and r-0.958, p-0.001 in the right kidney). Our findings support the notion of promoting Tc-99m MAG3 dynamic scintigraphy as an initial nuclear medicine technique in the diagnosis of the majority of kidney illnesses by giving information on differential renal function, cortical anomalies, and drainage at the same time.

Keywords: Renal Function, Renal Cortical Scar, Pediatric Population

1. Introduction

Kidneys are paired excretory organs responsible for maintaining body homeostasis. Any deviation of its function causes hemodynamic instability. Renal disease is considered a significant cause of morbidity and mortality in children. The prevalence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) are rising [1]. This rising burden mostly affects the developing countries [2]. Globally the prevalence of CKD in childhood has been reported as 15 to 74.7 per million children. CKD developed at the pediatric age also influences the adulthood of a child [3]. So early identification of the children at increased risk of renal diseases is mandatory for early interventions that could reduce the incidence of progressive chronic kidney disease and its associated complications. Renal scintigraphic approaches, both static and dynamic, have played an important role in the therapy of many renal disorders, offering a sensitive tool for illness identification even before structural alterations become visible. It is also advantageous that tracers for renal scintigraphy have substantially lower nephrotoxicity than X-ray contrast [4]. Tc-99m scan of the kidneys For more than 40 years, DMSA has been regarded the gold standard procedure for assessing renal cortical scar and estimating DRF [5, 6]. Tc-99m DMSA is a renal cortical binding agent that is actively taken up by the viable proximal and distal renal tubular cells, and then approximately 2 hours after injection, 40-60% of injected activity accumulates in the renal cortex and helps in gathering a large number of counts for imaging. This improves the statistical value for any given injected activity and enables detailed scintigraphy evaluation [7, 8]. The use of Tc-99m MAG3 as a dynamic agent increased significantly since its introduction in 1986 [9]. Because to the presence of Tc-99m, it gives greater picture quality than 1-131 ortho-iodohippurate (OIH). It is also recommended over DTPA (diethylenetriaminepentaacetic acid) for delivering well-delineated pictures due to more effective renal extraction (50-60%), particularly in newborns and young children, as well as those with compromised renal function [10]. In many countries including Bangladesh, both static and dynamic renal scintigraphies are performed to get information on DRF, cortical integrity, and urodynamics simultaneously which requires at least two days of procedures. It is also inconvenient and time-consuming for the patients to visit the hospital twice.

2. Objectives

2.1. General Objective

To evaluate the efficacy of Tc-99m MAG3 renal scintigraphy in calculating differential renal function (DRF) and detection of renal cortical scar in the pediatric population.

2.2. Specific Objectives

1) To estimate differential renal function (DRE) by Tc-99m MAG3 scintigraphy and Tc-99m DMSA scan.
2) To detect renal cortical scar by Tc-99m MAG3 scintigraphy and Tc-99m DMSA scan.
3) Agreement assessment between Tc-99m MAG3 scintigraphy and Tc-99m DMSA scan for the measurement of DRF.
4) Agreement assessment between Tc-99m MAG3 scintigraphy and Tc-99m DMSA scan for the detection of renal cortical scars.

3. Methodology and Materials

This cross-sectional observational study was carried out at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), Bangabandhu Sheikh Mujib Medical University (BSMMU) Campus, Shahbag, Dhaka, from July 2017 to June 2018. A total of 54 pediatric patients of different renal diseases were enrolled from NINMAS, BSMMU in the present study according to the selection criteria. The sampling technique was convenient and purposive sampling. Proper clinical history was taken and anthropometric measurements (age, height, and weight) were recorded in a structured datasheet. Prior to the commencement of this study, proper ethical approval and permission were taken from the respective departments. Informed written consent was collected from each of the participants. Each patient underwent both Tc-99m MAG3 scintigraphy and Tc-99m DMSA scan, performed on two separate days, a maximum of 7 days apart. Quantitative analysis was done for the calculation of DRF which was considered normal if the value remains within 45% to 55%. The reduced relative function of the kidney below 45% (that is more than a 10% difference between two kidneys) was considered abnormal. DRF values obtained by two methods were analyzed statistically by Pearson's correlation and Bland-Altman analysis. The independent t-test was used to compare the mean difference of DRF obtained by two methods. The statistical analysis was carried out using the SPSS version 22.0. Quantitative variables were expressed as mean ± standard deviation. An unpaired t-test was done to evaluate the mean difference. Pearson's correlation coefficient was done in between the DRF measured with DMSA scan and MAG3 scintigraphy methods and was shown in a scattered diagram. A Bland-Altman plot was used in analyzing the agreement between the differences of DRF, measured with two methods. Qualitative variables were expressed as frequencies and percentages. Test of significance was performed by Chi-square test for qualitative variables as well as kappa agreement analysis was done for a measure of agreement. A p-value of 0.05 or less was considered significant.

3.1. Inclusion Criteria

Patients with different renal disorders in pediatric age (up to 18 years).

3.2. Exclusion Criteria

i. Solitary kidney.
ii. History of nephrectomy.
iii. Pregnancy and Lactation.

4. Results

Table 1 shows the distribution of patients based on age, it was observed that almost half (46.3%) of patients belonged to the age group of 1 month -3 years. The mean was 4.57±4.40 years ranging from 0.08 to 18 years.

Figure 1 shows the gender distribution of studied patients. It was observed that almost three fourth (72.2%) of the patients were male and 15 (27.8%) were female. The Male-Female ratio was 2:6:1.

***Table 1.** Distribution of the study population by Age (n=54).*

Age (in year)	Number of patients	Percentage	Mean± SD	Range (Min-Max)
1 month–3 years	25	46.3		
>3–6 years	13	24.1		
>6-9 years	8	14.7		
>9-12 years	6	11.1	4.57±4.40	0.08-18
>12-15 years	1	1.9		
>15-18 years	1	1.9		
Total	54	100		

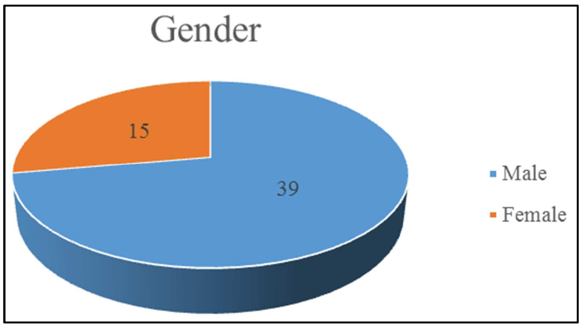

***Figure 1.** Gender distribution of the studied population (n=54).*

***Table 2.** Distribution of the studied patients by height & weight (n=54).*

	Mean ± SD	(min- max)
Height (cm)	96.70±31.70	30.5-157.5
Weight (kg)	16.97±11.95	2.7-47.6

Table 2 shows the distribution of patients on the basis of height and weight. It was observed that the mean height was 96.70 ± 31.70 cm with a range of 30.5 to 157.5 cm. The mean weight was 16.97 ± 11.95 with a range of 2.7 to 47.6 kg.

***Table 3.** Distribution of the study population by diagnosis (n=54).*

Diagnosis	Number of patients	Percentage
Hydronephrosis	27	50.0
VUR	7	12.96
UTI	6	11.11
Post pyeloplasty	4	7.41
CKD	3	5.56
Renal ectopia and fusion	3	5.56
Multicystic dysplastic kidney	1	1.85
Bladder Outlet Obstruction	1	1.85
Nephrotic Syndrome	1	1.85
IgA nephropathy	1	1.85
Total	54	100

Table 3 shows the clinical diagnosis of the studied patients. It was observed that 27 (50%) patients had hydronephrosis, 7 (12.9%) patients had VUR, 6 (11.1%) had UTI, and 4 (7.41%) patients in post pyeloplasty state follow up and 3 (5.56%) had chronic kidney disease.

***Table 4.** Distribution of the study population by history of operation (n=54).*

History of Operation	Number of patients	Percentage
No H/O Operation	43	79.5
Pyeloplasty	5	9.3
Fulguration	3	5.6
H/O Ureteric Reimplantation	2	3.7
Urethroplasty	1	1.9
Total	54	100

Table 4 shows the history of operation of the study population. It was observed that the majority (79.5%) of the patients had no history of operation, followed by 5 (9.3%) pyeloplasty, 3 (5.6%) fulguration, and 2 (3.7%) H/O ureteric reimplantation and 1 (1.9%) urethroplasty operation.

***Table 5.** Comparison of mean DRF measured by Tc-99m DMSA and Tc-99m MAG3 (n=54).*

Differential renal function in percentage	Tc-99m DMSA	Tc-99m MAG3	P value
	Mean± SD%	Mean± SD%	
Left kidney	54.22±20.38	51.47±23.88	0.521^{ns}
Right kidney	45.78±20.38	48.51±23.88	0.524^{ns}
ns= not significant			
p-value reached from unpaired t-test			

Table 5 shows differential renal function expressed in the percentage of the study population. It was observed that the mean DRF in the left kidney was 54.22±20.38% measured by Tc-99m DMSA and 51.47± 23.88% by Tc-99m MAG3. Mean DRF in the right kidney was 45.78±20.38% using Tc-99m DMSA and 48.51±23.88% using TC-99m MAG3. The difference was statistically not significant (>0.05) between the two groups.

Figure 2 shows a positive correlation between the DRF measured by Tc-99m MAG3 and Tc-99m DMSA scintigraphy in LK. Here, r=0.948 (r-value is closer to ±1), which is statistically significant with a strong correlation of the DRF, measured by the two different radiotracers.

Figure 3 shows a positive correlation between the DRF measured by MAG3 and DMSA scintigraphy in RK. Here, r=0.958 (r-value is close to ±1), which is statistically significant with a strong correlation of the DRF, measured by the two different radiotracers.

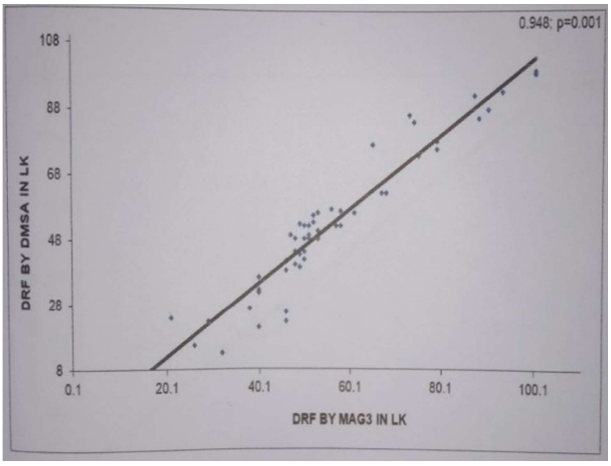

Figure 2. *The Scatter diagram shows a positive significant correlation (0.948; p=0001) between MAG3 and DMSA in the measurement of DRF in the case of the left kidney (LK).*

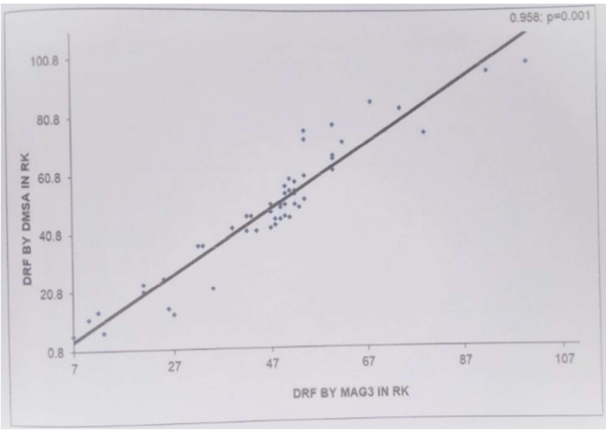

Figure 3. *Scatter diagram shows a positive significant correlation (0.948; p=0001) between MAG3 and DMSA in the measurement of DRF in the case of the right kidney (RK).*

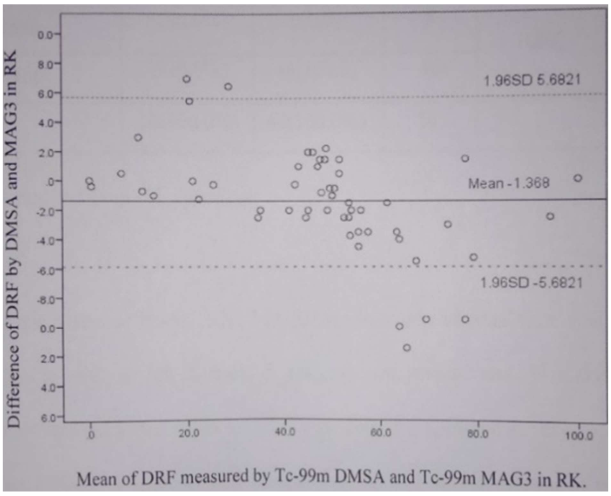

Figure 4. *Scatter diagram showing agreement between Tc-99m DMSA and Tc-99m MAG3 in the measurement of DRF in LK.*

Figure 4 displays a scatter diagram of the differences, plotted against the average of DRF, evaluated by T-99m DMSA and Tc-99m MAG3 in LK. Horizontal lines are drawn at the mean difference and at the limits of agreement, which are defined as the mean difference plus and minus 1.96 times the standard deviation of the differences. Bland-Altman plot for Tc-99m DMSA and Tc-99m MAG3 on behalf of DRF measurement in LK shows the mean difference of Tc-99m DMSA and Tc-99m MAG3 was 1.3769±3.5906%. 95% of differences were found between -5.660% and 8.414%.

$$d - 1.96\ s = 1.3769 - (1.96 \times 3.5906) = -5.660$$

$$d \pm 1.96\ s = 1.3769 \pm (1.96 \times 3.5906) = 8.414$$

Where, d = mean difference between Tc-99m DMSA and Tc-99m MAG3.

s= standard deviation.

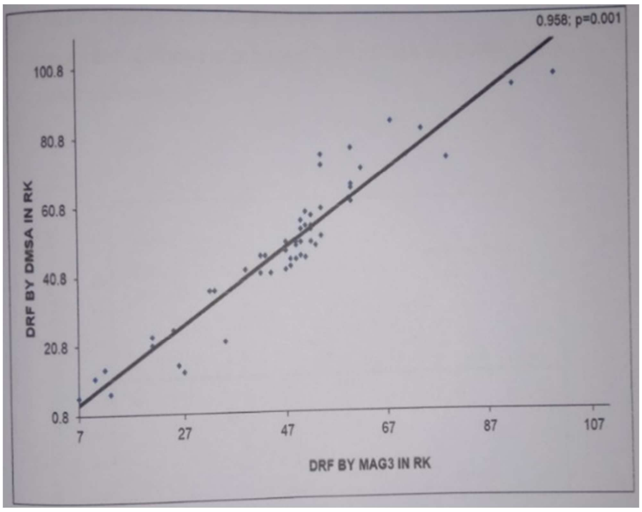

Figure 5. *Scatter diagram showing agreement between the DMSA and MAG3 in the measurement of DRF in RK.*

Figure 5 displays a scatter diagram of the differences, plotted against the average of DRF, evaluated by Tc-99m DMSA and Tc-99m MAG3 in RK. Horizontal lines are drawn at the mean difference and at the limits of agreement, which are defined as the mean difference plus and minus 1.96 times the standard deviation of the differences. Bland-Altman plot for Tc-99m DMSA and Tc-99m MAG3 on behalf of RK measurement shows the mean difference of Tc-99m DMSA and Tc-99m MAG3 was -1.368± 3.5975%. 95% of differences were found between -5.6821% and 5.6821%.

Agreement between DMSA with MAG3 in the evaluation of renal scar was measured by kappa statistics. In the case of the left kidney, 5 subjects had present and 49 had absent. Measures of agreement showed a kappa value of 0.867 with p<0.05 considered a very good agreement (Table 6).

Table 6. *Agreement between DMSA with MAG3 in the evaluation of renal scar (n=54).*

Renal scar (MAG3)	Renal scar (DMSA)			Kappa value	p-value
	Present	Absent	Total		
Left Kidney					
Present	5 (83.3%)	0 (0.0)	5		
Absent	1 (16.7%)	48 (100.0%)	49	0.899	0.001[s]
Total	6 (100.0%)	48 (100.0%)	54		
Right kidney					
Present	8 (80.0%)	0 (0.0)	8		
Absent	2 (20.0%)	44 (100.0%)	46	0.867	0.001[s]
Total	10 (100.0%)	44 (100.0%)	54		

s= significant
p-value reached from the chi-square test

5. Discussion

In this study, the unpaired t-test showed the mean difference of DRF measured by Tc-99m DMSA scan (mean 54.22% ± 20.38) and Tc-99m MAG3 renography (51.47% ± 23.88) were statistically not significant (p>0.05) in left kidney. There was a positive significant correlation between the two methods (Pearson correlation test, r=0.948, p=001). In Bland-Altman analysis, the mean difference of DRF measured by DMSA and Tc-99m MAG3 was 1.3769 ± 3.5906% with 95% of differences found between between-5.660% and 8.414%. The mean difference in DRF between DMSA and MAG3 was small. The bias between the methods was considered not significant. Similarly, in the case of the right kidney, the difference in DRF mean values were measured by two methods (Tc- 99m DMSA 45.78% ± 20.38 and Tc-99m MAG3 and 48.51% ± 23.88) were not statistically significant (p>0.05). There was a positive significant correlation between the two methods (Pearson correlation test, r=0.958, p= 0.001). In Bland-Altman analysis, the mean difference of DRF measured by Tc-99m DMSA and Tc-99m MAG3 was -1.368 ± 3.5975% with 95% of differences found between -5.6821% and 5.6821%. The mean difference of DRF between Tc-99m DMSA and Tc-99m MAG3 were small. The bias between the methods was considered not significant. These findings corresponded with the findings of multiple different studies [11-13]. All of the investigations showed that there was no statistically significant difference in DRF estimate between Tc-99m DMSA and Tc-99m MAG3, and there was a strong correlation between the two approaches. Othman et al. [14], in their study, reported that in 46 out of 52 patients, a Tc-99m MAG3 renogram could accurately measure DRF. Dostbil [15] reported in their study that the Bland-Altman plot demonstrated perfect agreement of the Tc-99m MAG3 and the Tc-99m DMSA methods in the calculation of DRF. We observed that the evaluation of Tc-99m MAG3 for detecting cortical scar in comparison to Tc-99m DMSA shows very good agreement with a kappa value of 0.899 on left kidneys and that of 0.867 on right kidneys. In the case of the left kidney, a Tc-99m DMSA scan revealed 6 kidneys having renal scars. In contrast, Tc-99m MAG3 was able to verify 5 (83.3%) kidneys. In the case of the right kidney, out of 10 DMSA detected scars, MAG3 could detect 8 (80.0%). MAG3 could diagnose cases of absent renal scar which was also established as an absent renal scar by DMSA for both left and right kidneys. A similar type of finding was found in the study of Abdulrezzak [11] in detecting renal parenchymal abnormalities. They found a high association between two radiotracers with a kappa value of 0.895. Some other studies also found that Tc-99m MAG3 has a high probability of assessing cortical defects in comparison to Tc-99m DMSA [16, 17]. MAG3 scintigraphy was also recommended as an initial screening test for children in some other studies [13, 14]. But contradicting results were found in the study by Piepsz [18]. In right-sided kidneys, DMSA detected 6 renal scars whereas Tc-99m MAG3 detected 4 (66.67%) renal scars with a kappa value of 0.780 with p<0.05 considered a good agreement. Two scars which were failed to be explored by Tc- 99m MAG3 were located on the upper pole. Failure of detection of scar in the parenchymal phase of Tc- 99m MAG3 was probably related to data acquisition. The images were acquired in only the posterior view with the use of a highly sensitive collimator, and low count due to a shorter acquisition period (2 to 3 minutes), all of which lead to a reduced Image resolution. Static images by DMSA Scan were acquired in different projections on a high-resolution collimator for a relatively prolonged period of time. Unidentified upper pole scars of right kidneys may be the consequence of superimposition of hepatic uptake of Tc-99m MAG3 over right renal activity, though a study by Arroyo reported that gallbladder uptake of 99mTc-MAG3 is S sporadic and minimal, with no adverse effects in the diagnostic and quantitative analysis of renal function, rather they advised for efficient MAG3 labeling, ensuring non-fasting state and additional studies with right angle detector [19].

Limitations of the Study: In this study, cases were selected from a single institute with a small sample size within a short period.

6. Conclusion

The present study demonstrated that the evaluation of Tc-99m MAG3 scintigraphy allows nearly the same information on differential renal function of each kidney as Tc-99m DMSA scintigraphy. In cortical scar detection, it provided adequate images for detecting most of the renal cortical scars in comparison to the Tc-99m DMSA scan at a lower dose of ionizing radiation, simultaneously delivering more information about perfusion, excretion, and collecting system. Therefore, all the renal information can be obtained by performing a single test, thereby reducing time and radiation burden.

7. Recommendation

The study was an instructive research-based study. Further research with proper follow-up should be conducted in the future. It is also recommended to enroll a large sample size in future studies to achieve results that are more consistent with normal distribution and include more symptomatic cases for evaluation of parenchymal abnormalities.

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