Study on Incidence of Contrast Induced Nephropathy (CIN) in Patient undergone CT Angiography in a hospital of Dhaka city, Bangladesh

A Dissertation Submitted to

East West University, Dhaka, Bangladesh

In the partial fulfillment of the requirements for the Degree of

Bachelor of Pharmacy

Submitted by

Md. Shahadat Hossain

ID: 2011-3-70-035

Under the Guidance of

Dr. Sufia Islam

Professor

Department of Pharmacy

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December, 2016

Declaration by the Research Candidate

I, Md. Shahadat Hossain, ID: 2011-3-70-035, hereby declare that the dissertation entitled--- "Study on Incidence of Contrast Induced Nephropathy (CIN) in patient undergone CT Angiography" submitted by me, has been carried out under the joint supervision and guidance of Dr. Sufia Islam, Professor and Dr. Bishwajit Bhowmik, Associate Professor of Bangabandhu Sheikh Mujib Medical University, to the Department of Pharmacy, East West University in partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy. It is further declared that the research work presented here is orginal, has not been submitted anywhere else for any degree or diploma.

……..

Md. Shahadat Hossain

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Certificate by the Supervisor

This is to certify that the thesis entitled "Study on Incidence of Contrast Induced Nephropathy (CIN) in patient undergone CT Angiography" submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bona fide record of original and genuine research work carried out by Md. Shahadat Hossain, ID: 2011-3-70-035 in 2016 of his research in the Bangabandhu Sheikh Mujib Medical University, under the supervision and guidance of me.

……..

Sufia Islam,

Professor

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Dhaka, Bangladesh.

Certificate by the Co-Supervisor

This is to certify that the thesis entitled "Study on Incidence of Contrast Induced Nephropathy (CIN) in patient undergone CT Angiography" submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bona fide record of original and genuine research work carried out by Md. Shahadat Hossain, ID: 2011-3-70-035 in 2016 of his research in the Bangabandhu Sheikh Mujib Medical University, under the co-supervision and guidance of me.

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Certificate by the Chairperson

This is to certify that the thesis entitled "Study on Incidence of Contrast Induced Nephropathy (CIN) in patient undergone CT Angiography" submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bona fide record of original and genuine research work carried out by Md. Shahadat Hossain, ID: 2011-3-70-035 in 2016 of his research in the Bangabandhu Sheikh Mujib Medical University.

…….

Dr. Shamsun Nahar Khan

Associate Professor and Chairperson

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Acknowledgement

At first I am grateful to Most Gracious Most Merciful ALLAH for the good health and well-being that were necessary to complete this research. Secondly, I would like to express my gratitude to my research supervisor, Dr. Sufia Islam, Professor of Department of Pharmacy, East West University, and co-supervisor Dr. Bishwajit Bhowmik, Assistant Professor of Bangabandhu Sheikh Mujib Medical University, who had been always optimistic and full of passion and ideas. My supervisor'S generous advice, constant supervision, intense support, enthusiastic encouragements and reminders during the research work not only helped shape this study but also molded me into being a better researcher. Her in-depth thinking, motivation, timely advice and encouragement have made it possible for me to complete this research.

Thirdly, I am also endebted to the Department of Pharmacy, East West University. I am very proud to be a part of this institution. To me it seems like second home. This institution gave me an opportunity to learn about my future goals, to learn how to show respect to the pharmacy profession. I would like to show my gratitude to the Chairperson of Pharmacy Department, to the faculties who are teaching over the last five years to make us ready for the noble profession by becoming a pharmacist.

Finally, I am immensely thankful to my beloved parents, Md. Abdus Sattar and Shahida Begum for their love and faith in me, especially for their unconditional love in my life. It is my parents who made who I am now. I also would like to express my genuine love to my other family members for their continuous support and love. I am fortunate to have such a nice family.

Dedication

To

My Beloved

Parents, Research Supervisors &

All EWUians

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Abstract

Contrast induced nephropathy (CIN) is a common hospital acquired acute kidney injury. It has been shown from different studies that this condition have dramatically increased in recent years. Intravenous contrast is used in Computed Tomography to help highlight blood vessels and to enhance the tissue structure of various organs such as the brain, spine, liver and kidneys. It is used in Computed Tomography Angiography. With the rise of the use of intravenous iodinated contrast media for both computed tomography scan and angiographic studies, there is a greater likelihood of adverse effects. One of the most well-known adverse effects of contrast is contrast induced nephropathy (CIN). CIN is defined as an absolute (>0.5 mg/dl) or relative (25%) increase in serum creatinine (SCr) within 48-72 hours after administration of iodinated contrast medium. The objective of this study is to determine the CIN among patients those are treated with contrast media before undergoing CT angiography. Twenty eight patients were enrolled in the outer patient clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka city, Bangladesh. All the patients were administered IV iodinated contrast before the process of angiography. The serum creatinine level were measured before the administration of contrast. The average serum creatinine level at 0 hour is 0.9427±0.2348 mg/dl and 48hours of contrast administration is 0.9900±0.2451 mg/dl. There is no significant difference ($p = 0.4763$) between the creatinine level before (0 hr) and after (48 h) administration of contrast. This study shows that acute kidney injury is not found in these patients who were undergone CT angiography.

Chapter 1

Introduction and Literature Review

1. Introduction

The administration of intravenous iodinated contrast media has been of great value to the practice of radiology, but it is not without risks. Major risk is contrast induced nephropathy(CIN).CIN has been associated with an increase in morbidity, mortality, as well as prolonged hospital course. It is believed to account for nearly 10% of hospital acquired acute renal failure.CIN can occur in many patients who have previous renal problem. This work will discuss about the contrast induced nephropathy in Bangladeshi patients who have undergone CT angiography in a hospital in Dhaka city.In this study we used iodine based Iopamidol as a contrast agent.

1.1. Contrast induced Nephropathy(CIN)

Contrast Induced Nephropathy is defined as an absolute (>0.5 mg/dl) or relative (25%) increase in serum creatinine (SCr) within 48-72 hours after iodinated contrast medium administration in the absence of any other explanation for the rise in SCr. SCr will usually peak at 2-3 days following contrast media use and then returns slowly to baseline within 14 days. Yet, some patients progress quickly to acute renal failure, which may require hemodialysis.

Acute renal failure is defined as the increase in creatinine level of more than 0.3 mg/dl within 48 hours, an increase of more than 50% of the baseline creatinine level within 7 days, or oliguria lasting for more than 6 hours. The grave concern with acute renal failure is that it is also associated with a mortality of 40%-90%. (Nicola et al., 2015).

1.2. Complications of CIN

Diagnostic radiographic imaging scans using intravascular iodinated contrast media can lead to various complications. One of the leading causes of hospital-acquired acute kidney injury is CIN. This is one of the most important possible complications after angiography. There are several risk factors of using contrast. They are - longer hospital stays, renal dysfunction, poor long term clinical outcomes, increased morbidity and mortality. Diabetes mellitus, hypercholesterolemia and underlying chronic kidney disease are the major risk factors of administration of contrast for procedures (Khosravi et al., 2016).

Most of the physicians who refer patients for the diagnosis and who perform the diagnosis are not so well known about CIN. They are not fully informed about the risk of CIN. A survey found that less than half of referring physicians were aware of potential risk factors, including diabetes mellitus. The most important protective intervention is hydration both before and after the radiographic imaging scan (Gallegos et al., 2016).

Etiology of CIN

Contrast media act on individual anatomic sites within the kidney and exert adverse effects by multiple mechanisms. As a result a direct cytotoxic effect occur on the renal proximal tubular cells,enhance cellular damage by reactive oxygen species, and increase resistance to renal blood flow. They also enhance renal vasoconstriction, particularly in the deeper portions of the outer medulla. This is especially important in patients with Chronic Kidney Disease (CKD), because their preexisting abnormal vascular pathobiology is made worse by the effects of contrast media.

1.3. Risk factors of CIN

The most important predictor of CIN risk is chronic kidney disease (CKD). Patients with CKD have an increased risk by more than 20 times that of a normal individual to develop CIN. Patients with a glomerular filtration rate (GFR) <30 mL/min at the time of contrast administration are also at the highest risk. In addition, following are the strong risk factors.

- Pre-existing condition of renal insufficiency (SCr level >1.5 mg/dl),
- Diabetes mellitus,
- Sepsis,
- Hypotension,
- Dehydration,
- Cardiovascular disease,
- Use of diuretics,
- Advanced age (>70 years),
- Organ transplant,
- Myeloma,
- Hypertension, and
- Hyeruricemia

The risk of CIN has been associated with composition of the contrast agent such as non-ionic or ionic, and monomer or dimmers. This is used to describe the ratio of iodine atoms to dissolved particles. The lower the ratio, the more concentrated the contrast agent and higher in osmolality. But it demonstrates good contrast opacification with the least toxic effect. The lower the osmolality of the contrast agent, the fewer the incidence of anaphylaxis and cardiovascular reactions occur. (Nicola et al., 2015).

Contrast Agent

Contrast agent used in medical imaging to enhance the contrast of structures or fluids within the body. It is commonly used to enhance the visibility of blood vessels and the gastrointestinal tract. Several types of contrast agent are used in medical imaging for diagnosis. They can be classified base on the imaging modalities where they are used. Although other types exist, most common contrast agents work based on X-ray attenuation and magnetic resonance signal enhancement.

X-ray attenuation

Iodine and barium are the most common types of contrast medium for enhancing x-ray-based imaging methods. Various sorts of iodinated contrast media exist, with variations occurring between the osmolarity, viscosity and absolute iodine content of different media. Non-ionic dimers are favored for their low osmolarity and toxicity, but have a correspondingly higher price attached to their use.

MR signal enhancing

Gadolinium is used in magnetic resonance imaging as a MRI contrast agent. In the 3+ oxidation state the metal has 7 unpaired electrons. This causes water around the contrast agent to relax quickly, enhancing the quality of the MRI scan.

In this study we used Iopamidol as a contrast agent.

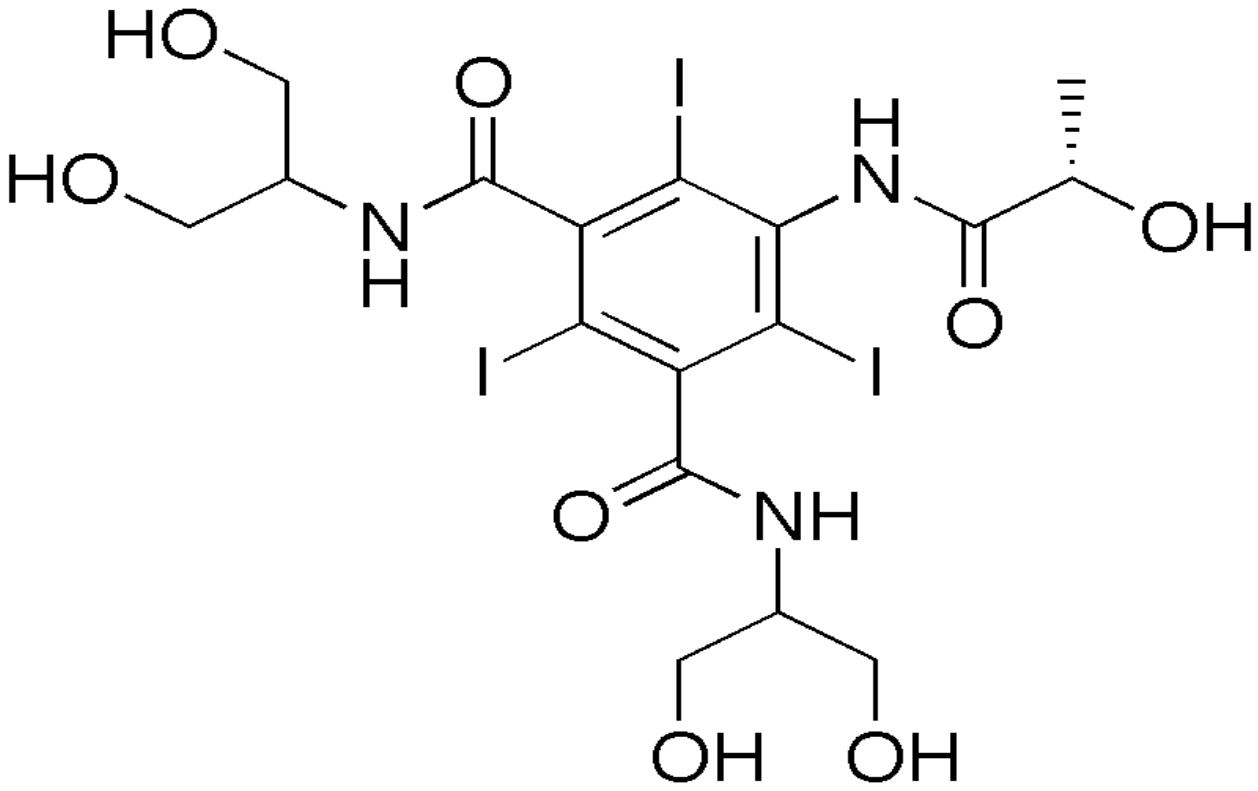
Iopamidol

Iopamidol contains iodine, a substance that absorbs X-rays. Radiopaque contrast agents are used to allow blood vessels, organs, and other non-bony tissues to be seen more clearly on a CT scan or other radiologic (X-ray) examination.

It is primarily used in:

- Angiography throughout the cardiovascular system, including cerebral and peripheral arteriography, coronary arteriography and ventriculography, pediatric angiocardiography, selective visceral arteriography and aortography, peripheral venography (phlebography).
- Adult and pediatric intravenous excretory urography and intravenous adult and pediatric contrast enhancement of computed tomographic (CECT) head and body imaging.

Structure:



IUPAC name: 1-N,3-N-bis(1,3-dihydroxypropan-2-yl)-5-[(2S)-2-hydroxypropanamido]-2,4,6-triiodobenzene-1,3-dicarboxamide.

Formula: C17H22I3N3O8

Molar mass: 777.08 g/mol.

Treatment Approach Considerations

The base of contrast-induced nephropathy (CIN) prevention in hydration therapy.

Following contrast administration renal perfusion is decreased for up to 20 hours.Intravascular volume expansion maintains renal blood flow, preserves nitric oxide production, prevents medullarhypoxemia, and enhances contrast elimination.

A number of other therapies for CIN have been investigated, including the hydration therapy, use of statin drugs, bicarbonate, N-acetylcysteine (NAC), ascorbic acid, the adenosine antagonists theophylline and aminophylline, vasodilators, forced diuresis, and renal replacement therapy. Patients with CIN should be managed in consultation with a nephrologist.

1.3.1. Hydration Therapy

Preprocedural hydration is the single most important measure to decrease the risk of CIN. Volume expansion inhibits the renin-angiotensin-aldosterone system, decreases the release of vasoconstrictors and reactive oxygen species production, and dowregulates the tubuloglomerular feedback. Hydration also decreases the direct toxic effects of CM in the kidney by diluting it (and decreasing its viscosity) within renal tubules. Several types of solutions, rates, durations, and routes of administration have been tested. A meta-analysis of 6 trials showed that oral hydration with a prespecified volume expansion is as effective as the intravenous route for CIN prevention (odds ratio, 0.75; 95% confidence interval [CI], 0.37-1.50; P=0.42). Hydration with isotonic saline (0.9% Nacl) is superior to half-isotonic saline (0.45% Nacl) (0.7% vs 2.0%; P=0.04), likely because of the former's greater ability to expand intravascular volume. Recently, Brar et al. reported that total hydration volume can be doubled by using a left ventricular end-diastolic pressure-guided hydration scheme, without compromising patient safety. This was associated with an absolute 10% reduction in the incidence of CIN and an absolute 6% decrease in the occurrence of a composite end point of death, MI, and the need for renal replacement therapy at 6 months. Regarding the relative advantage of sodium bicarbonate over sodium chloride, data from meta-analyses have been contradictory. There is no strong evidence of the benefit of the former over the latter (relative risk [RR], 0.85; 95% CI, 0.63-1.16). In light of

these data, current guidelines recommend hydration with normal saline from 12 hours before untile 24 hours after CM exposure at 1-1.5 mL/kg/h. (Azzalini et al., 2015)

1.3.2. Statin Drugs

Statin drugs have been shown to possess pleitopic effects, including enhancement of endothelial nitric oxide production and reduction of endothelin secretion, as well as anti-inflammatory and antioxidative properties. Han et al. randomized 2998 patients with diabetes and CKD to receive rosuvastatin 10 mg/d for 5 days (2 days before and 3 days after the procedure) or standard of care. Patients treated with rosuvastatin had significantly lower incidence of CIN (2.3% vs 3.9%; P=0.01). Similarly, Leoncini et al. randomized 504 patients with non-STEMI to receive rosuvastatin (40 Mg on admission, followed by 20 mg/d throught study period) or placebo. The incidence of CIN was significantly lower in the statin group (6.7% vs 15.1%; P=0.001), as was the 30 day incidence of a composite of death, dialysis, MI, stroke, or persistent renal damage (3.6% vs 7.9%; P=0.036). Finally, a meta-analysis of 8 randomized trials showed that periprocedural short-term use of high-dose statin drug was associated with a significant reduction of CIN (RR, 0.51; 95% Cl, 0.34-0.77; P=0.001). Given the available evidence, ESC guidelines have recommended short-term use of high-dose statin drugs before cardiac catheterization. (Azzalini et al., 2015)

Patients without history of renal disease, the risk of CIN is less than 1%. It was previously believed that patients without any history of pre-existing renal insuffeciency have 12%-27% of CIN, and if there was history of diabetic nephropathy, the incidence increases to 50%. The single most important predictor of CIN risk is chronic kidney disease (CKD). Patients with CKD have an increased risk by more than 20 times that of a normal individual to develop CIN. Also, patients with a glomerular filtration rate (GFR) < 30 mL/min at the time of contrast administration are also at the higher risk. The risk of CIN has been associated with composition of the contrast agent such as non-ionic or ionic, and monomer or dimers. This is used to describe the ratio of iodine atoms to dissolved particles. The lower the ratio, the more concentrated the contrast agent and higher in osmolality, but demonstrates good contrast opacification with the least toxic effect. However, the lower the osmolality of the contrast agent, the fewer the incidence of anaphylaxis and cardiovascular reactions occur.

There is also the guidelines for the prevention of CIN. Patients with a GFR > 60 mL/min have normal or near normal renal function and have very low risk of CIN and require no prophaylaxis or follow-up. With a GFR < 45-59 mL/min, there is a low risk of CIN in patients without risk factors. No specific prophylaxis or follow-up is required. For patients with receive intra-arterial contrast media preventative measures are recommended. If the GFR < 45 mL/min, patients are at moderate risk for CIN and preventative measures are recommended. IV hydration is recommended for patients who receive intra-arterial contrast. For IV administration, either oral or IV hydration can be used. (Nicola et al., 2015)

CIN can result from intravenous or intra-arterial injections of iodine-based contrast media(CM) during enhanced X-ray and computerized tomography (CT) imaging examinations, or coronary artery interventions (Chang and Lin, 2013). The reported risk factors are summarized in Table-1.

Table-1

Risk factors for contrast induced nephropathy	
Patient-related risk factors	**Procedure-related risk factors**
Preexisting kidney disease. Diabetes with chronic kidney disease. Age > 75 y. Dehydration. Hypoalbuminemia (<35 g/L). Poor heart function or hemodynamic instability. Preprocedure intra-aortic balloon pump. Anemia or postprocedure drop in hematocrit. Hypotension. Advanced heart failure. Left ventricular ejection fracture <40%.	Type of CM High-osmolar CM Ionic vs. non-ionic CM High-viscosity CM High volume of CM Multiple CM injections within 72 h. Intra-arterial vs. intravenous injection.
	Conflicting (doubtful) risk factors

Acute myocardial infarction or increased CK-MB. Need for cardiac surgery after contrast exposure. Urgent or emergent procedure. Peripheral vascular disease. Concurrent nephrotoxic medication. NSAIDs, aminoglycoside, amphotericin B, high-dose diuretics, antiviral drug such as acyclovir and foscarnet, cyclosporine A.	Female. Multiple myoloma. Cirrhosis. Use of ACEI or ARB. Renal transplant. Diabetes with normal renal function. Low-osmolar CM in high-risk patients.

The pathogenesis of CIN is still not completely understood, although it is clear that the root concept is medullary hypoxia-induced renal tubular damage. Whereas an interaction of various mechanisms has been shown to cause CIN, a reduction in renal perfusion and toxic effects on the tubular cells caused by direct and indirect effects of the CM on the kidneys are generally recognized as important mechanisms (Table-2).

Table-2

Possible mechanisms of contrast induced nephropathy
Medullary hypoxia resulting in renal tubular necrosis
Rheologic alteration-viscosity Osmotic load-increased demand Vasoactive mediator imbalance Drecreased vasodilators Increased vasoconstrictors Systemic hemodynamic instability
Direct tubular cytotoxicity

Apoptosis through mitochondrial pathway
Generation of ROS
Increased adenosine from endothelial cells
Medullary hypoxia
ROS block nitric oxide vasodilatation effect
ROS result in vasoconstriction

ROS= reactive oxygen species.

To our knowledge no study has been carried out to detect contrast induced nephropathy in Bangladeshi patients undergone CT angiograohy. Therefore, this study has been carried out to detect contrast induced nephropathy in Bangladeshi patients undergone CT angiograohy.

Chapter 2

Objective of the Study

2.1. Research Objective

The objective of this analysis is to determine the Contrast Induced Nephropathy (CIN) among patients those are undergone CT angiography.

Chapter 3

Methodology

3.1. Research Methodology

PATIENTS' ENROLLMENT

Twenty eight patients were enrolled in this study. All of the patients underwent CT angiography for any cardiovascular disorder. A questionnaire was developed andsome selected questions were asked to the patients. The questions were about the daily life, previous disease and medicine history of the patients (Annexure 1). A consent form (Annexure 2) was given to all patients to confirm that he or she agrees to the procedure and is aware of any risks that might be involved in the procedure. An iodine based contrast agent eg. Iopamidol was used for the procedure.The amount of contrast was 70 to 80 ml. The CT angiography was done on individual patient for diagnosis purpose.

Before contrast administration the serum creatinine level was measured. After serum creatinine level was measured again to see whether the patients' creatinine level was within the normal range.

Serum-Creatinine measurement:

Test Principle

Creatinine is produced as a waste product of creatine and phosphocreatine. Because much of the creatinine is produced in muscle, the amount of creatinine that is measured in blood is proportional to the patient's lean muscle mass. The waste product creatinine, enters the blood supply and is excreted in the urine. The measurement of creatinine is used to aid in the determination of renal function. The principle of the measurement of creatinine is based on the Jaffe reaction. That is, under alkaline conditions creatinine reacts directly with picric ions forming a reddish complex, the absorbance of which can be measured at 520 nm. However, several interfering substances including proteins, ketones, glucose, and ascorbic acid also react with picric acid, producing similar colored complexes. Serum proteins are precipitated with tungstic acid solution before measuring for creatinine.

Specimen

Fresh serum or serum stored up to four weeks at 2 to 8°C. Frozen serum can be used if gently thawed and thoroughly mixed prior to use.

Reagents and Equipment

1. Spectrophotometer
2. Spectrophotometer cuvettes
3. 5 mL test tubes
4. Pipettes
5. Paraffin squares
6. Timer
7. Distilled deionized water
8. Picric acid, 0.036 mol/L. 9.16 g reagent grade picric acid was dissolved in warm water, cooled and made up to 1 L volume.
9. Tungstic Acid in Polyvinyl Alcohol. 1 g polyvinyl alcohol was placed in 100 mL water and heated to dissolve but didn't boil and transferred to a 1 L volumetric flask containing 11.1 g $Na_2WO_4 \cdot 2H_20$ in 300 mL of water. Then 2.1 mL concentrated H_2SO_4 was added in 300 mL water. Mixed, and diluted with water to 1 L volume. This solution is stable at room temperature (25°C) for 2 years and does not require refrigeration.
10. NaOH, 1.4 mol/L. 54 g NaOH was dissolved in water and diluted to 1 L volume and stored in a polyethylene bottle.
11. Creatinine standards, 0.5 mg/dL, 1.0 mg/dL, 2.0 mg/dL, 4.0 mg/dL, 10.0 mg/dL
12. Graph paper

Procedure

1. Spectrophotometer was turned on and warmed up for at least 15 minutes.
2. Wavelength was set at 520 nm.

3. Proteins were precipitated which is present in the patient serum specimens and in each control by adding 0.5 mL of the specimen to 4.0 mL tungstic acid in a test tube. Then it was shaken vigorously and centrifuge for 10 minutes.
4. Cuvettes were labelled from 1 through 10.
5. 1.0 mL of picric acid solution to cuvettes 1 through 10, was added.
6. 3.0 mL distilled deionized water to cuvette 1, was added. And also following additions were done-
7. 3.0 mL of the 0.5 mg/dLcreatinine standard to cuvette 2.
8. 3.0 mL of the 1.0 mg/dLcreatinine standard to cuvette 3.
9. 3.0 mL of the 2.0 mg/dLcreatinine standard to cuvette 4
10. 3.0 mL of the 4.0 mg/dLcreatinine standard to cuvette 5.
11. 3.0 mL of the 10.0 mg/dLcreatinine standard to cuvette 6.
12. 3.0 mL of the protein free centrifugate of control Level One to cuvette 7.
13. 3.0 mL of the protein free centrifugate of control Level Two to cuvette 8.
14. 3.0 mL of the patient's protein free serum or urine were centrifuged to the remaining cuvettes.
15. Then it was mixed by inversion using a paraffin square to prevent spillage.
16. 0.5 mL of the NaOH solution was added to the first cuvette. They were mixed and set a timer for 15 minutes.
17. 0.5 mL of the NaOH was added to the remaining cuvettes at 30 second intervals.
18. After 15 minutes, cuvette was placed in the spectrophotometer and set the Absorbance to read 0.000.
19. Absorbance was read at exactly 15 minutes after adding the NaOH and the Absorbance for cuvettes 2-10 was recorded

Reference Intervals

The reference range for serum creatinine is as follows:

	Reference Range
0-18 years	0.4-1.0 mg/dL
adult female	0.6-1.2 mg/dL
adult male	0.8-1.5 mg/dL

Result/Interpretation

1. Using graph paper, the Absorbance was plotted on the vertical (y axis) against the concentration on the horizontal (x axis) for each of the creatinine standards.
2. A "best fit line" was drawn and used this standard curve to determine the creatinine concentration for the controls and patient specimens.

Precaution:

Anhydrous picric acid is explosive. Picric acid crystals must never be desiccated or heated.
Creatinine is a chemical waste molecule that is generated from muscle metabolism. Chreatinine is transported through the bloodstream to the kidneys. The kidneys filter out most of the creatinine and dispose of it in the urine.(Charles Patrick Davis, 2016)

A creatinine blood test doesn't require very much preparation. It's important to tell the doctor about any prescription or over-the-counter medications patints are currently taking. Some drugs may increase creatinine levels without causing kidney damage and interfere test results. The creatinine blood test is a simple test that requires the removal of a small sample of blood.
A technician asked patient to pull up his/her sleeves so that patient'S arm is exposed. They did sterilize the injection site with an antiseptic and then tie a band around patient'S arm. This makes the veins swell with blood, allowing them to find a vein more easily. Once they find a vein, they'll insert a needle into it to collect the blood. In most cases, a vein on the inside of the elbow is used. Patient might feel a slight prick when the needle is inserted, but the test itself isn't painful. After the technician removes the needle, they'll put a bandage over the puncture wound.

A creatinine blood test is a low-risk procedure. However, there are some minor risks, including:

fainting at the sight of blood,
dizziness or vertigo,
soreness or redness at the puncture site,
bruising,
pain,
infection.

Once enough blood is drawn, the sample is sent to the laboratory for analysis. Creatinine is measured in milligrams per deciliter of blood (mg/dL). People who are more muscular tend to have higher creatinine levels. Results may also vary depending on age and gender.
In general, however, normal creatinine levels range from 0.7 to 1.3 mg/dL in men and 0.6 to 1.1 mg/dL in women.(Roth and Morrison, 2015)

Chapter 4

Result

4.1. Figure-1: Percentage of patients suffering from hypertension (n=28).

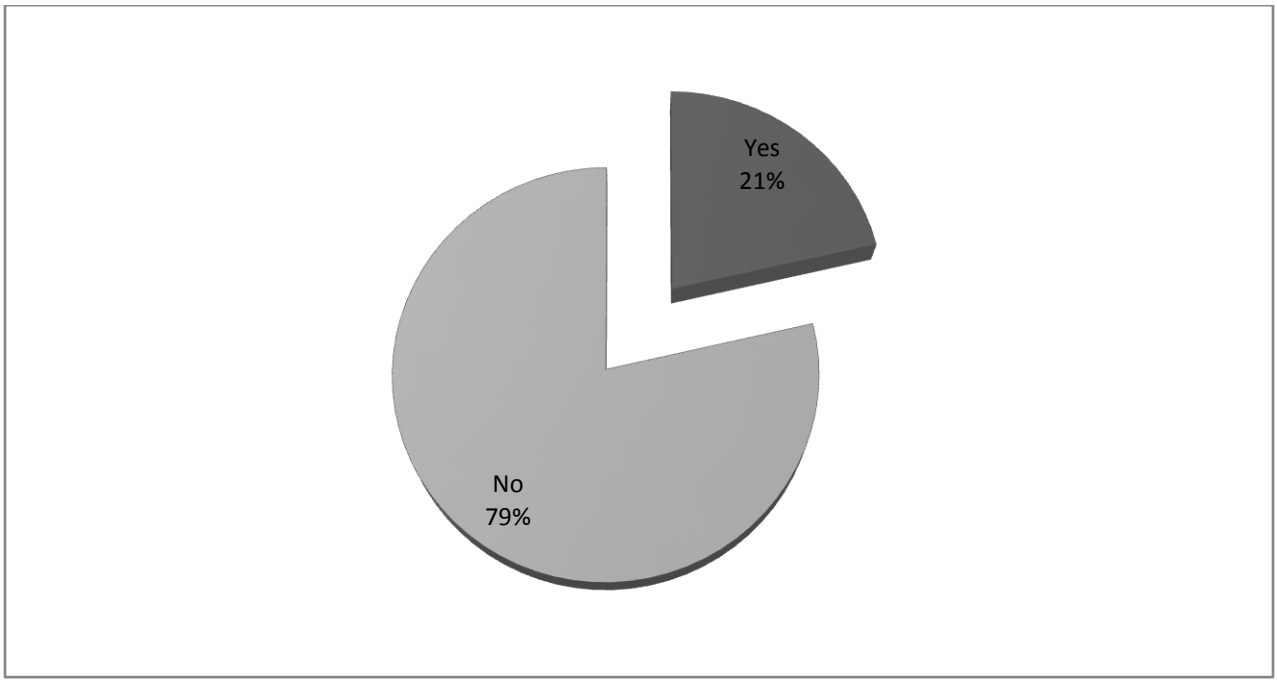


Figure-1 shows percent distribution of the patients suffering from hypertension. Among 28 patients undergone CT angiography,6 patients (21%) suffer from hypertension.

4.2. Table-3: Smoking habit of the patients (%) undergone CT angiography (n=28).

Table-3

No of patients	Smoking habit	Percentage
6	Yes	21.43%
22	No	78.57%

Table-3 shows that only 21% patients have smoking habit out of 28. All 28 patients have undergone CT angiography. Rest of the patients (79%) do not have smoking habit.

4.3. Figure-2: Age of Female (n=10) and Male (n=18) patients.

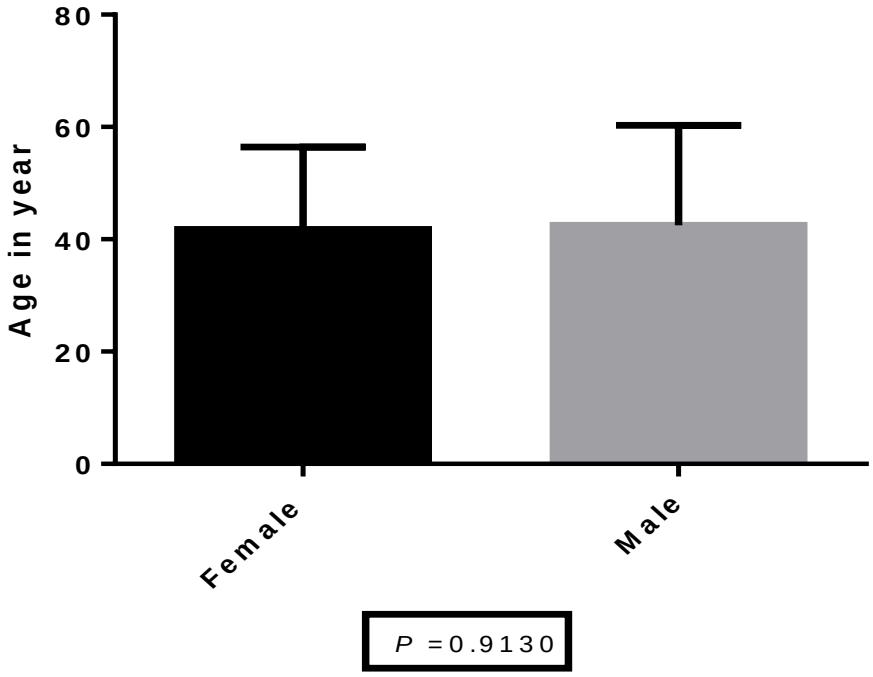


Figure-2 illustrates the age distribution of the female (n=10) and male (n=18) patients undergone CT angiography.

It is seen that the average age of female patients is 41.80±4.628 years. And the average age of male patients is 42.53±4.182. The age of male and female is not significantly different (p=0.9130).

4.4. Figure-3: Serum creatinine level at 0 h (n=28) and after 48 h (n=25) of contrast administration in all patients.

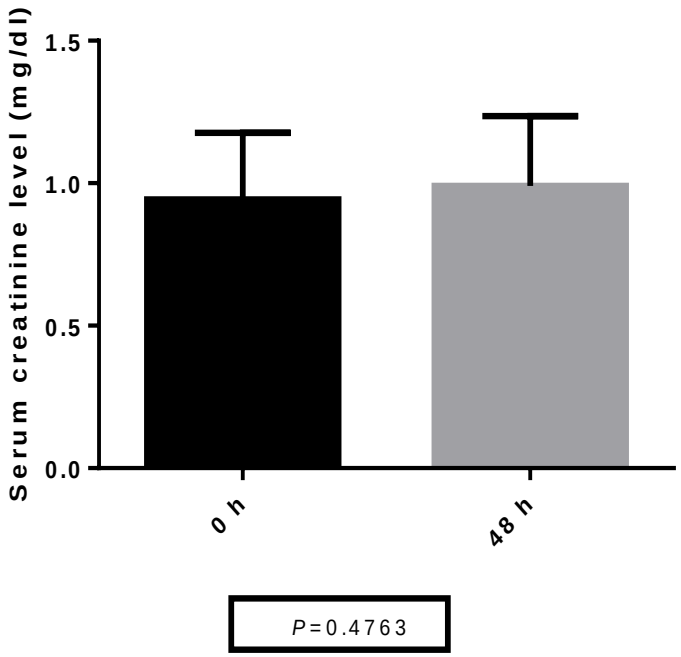
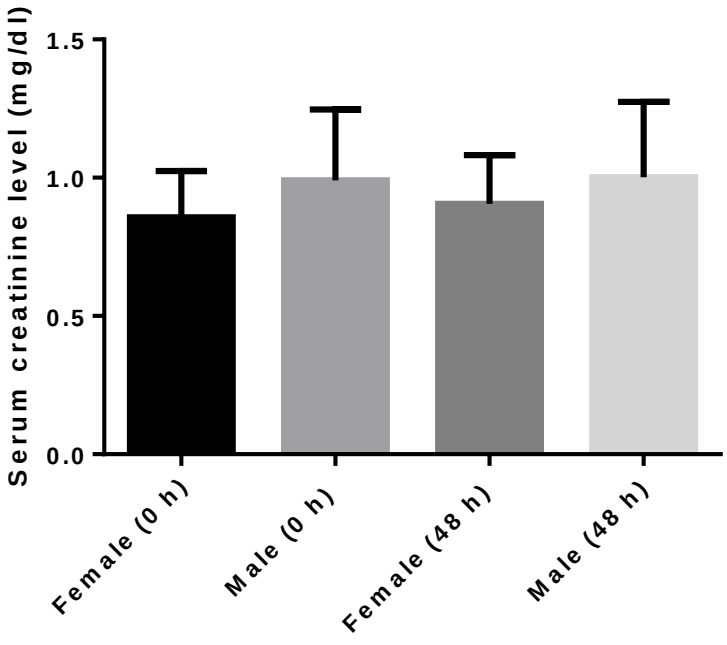


Figure-3 illustrates the serum creatinine level of patients at 0 hour (n=28) and after 48 hours (n=25) of contrast administration in all patients. The average serum creatinine level at 0 hour is 0.9427±0.2348 mg/dl. And the average serum creatinine level after 48hours of contrast administration is 0.9900±0.2451 mg/dl. There is no significant difference (p=0.4763) observed in terms of the serum creatinine concentration between 0 and 48 hours.

4.5. Figure-4: Serum creatinine level before and after administration of contrast in male and female patients.



Male (n=18, 17 at 0 and 48 h)
Female (n=10, 6 at 0 and 48 h)

None of the values are significantly different

Figure-4 illustrates the serum creatinine level of female patients at 0 hour (n=10) and after 48 hours (n=8) and male patients at 0 hour (n=18) and after 48 hours (n=17) of contrast administration in patients. The average serum creatinine level of female patients at 0 hour is 0.8565±0.1677 mg/dl. And the average serum creatinine level of female patients after 48 hours of contrast administration is 0.9050±0.1766 mg/dl. The average serum creatinine level of male patients at 0 hour is 0.9906±0.2567 mg/dl. And the average serum creatinine level of male patients after 48 hours contrast administration is 1.002±0.2726 mg/dl. None of the values are significantly different.

Chapter 5

Discussion

5.1. Discussion

Contrast induced nephropathy (CIN) is a common hospital acquired acute kidney injury. The incidence of CIN can be much higher if the patients have underlying conditions such as chronic kidney disease (CKD), diabetes, or old age. (Nicola et al., 2015). Published studies on this condition have dramatically increased in recent years. To our knowledge no stduty has been taken place until now in Bangladesh. We conducted this study where serum creatinine measurement is taken from the patients at 2 times. First creatinine level was measured at 0 hour and second one is after 48 hours of contrast administration.. Total 28 patints have been enrolled in this study. Among them 10 patients are female and 18 are male. Although 28 patients have serum creatinine level at 0 hours but 3 patients didn't appear after 48 hours. Among 28 patients undergone CT angiography, 6 patients (21%) suffer from hypertension and 6 patients (21%) have smoking habit. The average age of female patients was 41.80±4.628 years. And the average age of male was 42.53±4.182. The average serum creatinine level at 0 hour was 0.9427±0.2348 mg/dl and after 48hours of contrast administration was 0.9900±0.2451 mg/dl. There is no significant difference (p=0.4763) observed in terms of the serum creatinine concentration between 0 and 48 hours.

Seventy one patients were underwent CT angiography of the chest, abdomen, and pelvis as part of the cardiac workup before kidney transplantation. Volumetric bone mineral density (vBMD) of the lumbar spine (LS) and proximal femur were calculated before and after administration of 95 ml contrast intravenously. After contrast media administration vBMD increased both at the LS and proximal femur. Although the absolute difference was comparable, the relative difference was almost twice as high at the LS (10.2% [6.1-14.1]) compared to the total hip (TH) (5.9% [2.4-9.3], p<0.001) and femoral neck (FN) (5.3% [0.5-9.9], p <0.001). Women had a greater increase in LS-vBMD than men (13.4 ± 8.0 vs 9.8 ± 4.8 mg/cc, p + 0.02). In conclusion vBMD of the spine and hip increased after contrast media administration in a cohort of patients with chronic kidney disease. (Jorgensen et al., 2016)

Another article titled as 'Association of contrast-induced nephropathy with risk of adverse clinical outcomes in patients with cardiac catheterization: They evaluated the association between CIN and cardiovascular and renal events after cardiac catheterization. This study examined 853 patients undergoing cardiac catheterization from 27 hospitals. During follow-up

periods (477 ± 214 days), CIN, major adverse cardiovascular and cerebrovascular events (MACCE), and renal events occurred in 44 (5.2%), 71 (8.3%), and 26 (3.0%) patients, respectively. Kaplan-Meier analysis showed that CIN yielded increasing risk for MACCE, ADHF, newly-required hemodialysis, and renal events. (Sato et al., 2016)

It has been shown from randomized trials comparing iso osmolar contrast media (IOCM) to low osmolar contrast media (LOCM) in CKD stage 3 and above patients undergoing coronary angiography, and reporting incidence of CIN were included in the analysis. The secondary outcome of the study was the incidence of serum creatinine increase by >1 mg/dl. Two thousand eight hundred and thirty nine patients (2839) were included in 10 trials, in which 1430 patients received IOCM and 1393 received LOCM. When compared to LOCM, IOCM was not associated with significant benefit in preventing CIN (OR=0.72, [CI: 0.50-1.04], P=0.08, 12=59%). (Pandya et al., 2016).

In our study we have not seen any CIN in our patients after administration of contrast before CT angiography. We measured the creatinine level only after 48 hours of contrast administration. This study was done on only 28 patients and this small sample size can be a factor not to see any difference in patients regarding CIN.

Iodinated contrast media can lead to various complications when used for diagnostic purpose. CIN is one of the most important possible complications after angiography. There are several risk factors of usinf contrast which include longer hospital stays, renal dysfunction, poor long term clinical outcomes, increased morbidity and mortality. Diabetes mellitus, hypercholesterolemia and underlying chronic kidney after administration of contrast for procedures. (Khosravi et al., 2016).

To our knowledge, this is the first time we conducted study on CIN on 28 patients using only one contrast agent. Further study is needed with higher sample size with different contrast agents to determine the possibility of CIN undergone different diagnostic procedures.

Chapter 6

Annexure-1

Incidence/Previlence of Contrast Induced Nephropathy in the patient undergone CT Angiography in a hostpital of Dhaka city, Bangladesh

Dear Sir/Madam,

You are scheduled to undergo a CT Angiography on the __/__/__.

Name: Sex: □ Male □ Female

Please fill out the following questionnaire.

1. How old are you?

   _____

2. What is current Blood Pressure?

   _____

3. Have you ever suffered from an allergic reaction?

   □ Yes □ No

4. Do you currently or have you smoked tobacco during the previous month?

   □ Yes □ No

   If 'yes'

   a) At what age did you start smoking? _____
   b) How long ago did you quit smoking? _____
   c) How many packs per day did or do you smoke? _____

5. Do you suffer from diabetes?

   □ Yes □ No

   If 'yes'

   What are the drugs you take now?

   _____

6. Have you ever suffered from kidney disease?

   □ Yes □ No

   (If 'yes' please specify) _____

7. Do you suffer from any of the following disease?

   Heart failure □ Yes □ No

   High blood pressure □ Yes □ No

   High Cholesterol □ Yes □ No

   Gout □ Yes □ No

   Liver disease □ Yes □ No

   Multiple myeloma □ Yes □ No

8. What are the drugs you take now?

   _____

Serum Creatinine level

1. What is your current Serum Creatinine level? _____
2. After 48-72 hours: _____
3. After 1 week: _____

Chapter 7

Annexure-2

বঙ্গবন্ধু শেখ মুজিব মেডিক্যাল বিশ্ববিদ্যালয়

ঢাকা, বাংলাদেশ

স্বেচ্ছা-সম্মতি পত্র

গবেষণা শিরোনামঃ

রোগীর সিটি এনজিওগ্রাফী চলার সময় এর উপর কন্ট্রাস্ট ইন্ডিউসড নেফ্রপ্যাথীর প্রকোপ।

প্রধান গবেষকঃ ডাঃ বিশ্বজিত ভৌমিক

প্রতিষ্ঠানঃ১। বঙ্গবন্ধু শেখ মুজিব মেডিকেল বিশ্ববিদ্যালয়, বাংলাদেশ

২। গ্রীন লাইফ মেডিকেল কলেজ এন্ড হসপিটাল

গবেষণার ভূমিকাঃ

বঙ্গবন্ধু শেখ মুজিব বিশ্ববিদ্যালয়ে এবং গ্রীন লাইফ মেডিকেল কলেজ এন্ড হসপিটালে পরিচালিত একটি গবেষণা পরীক্ষাতে অংশ নেওয়ার জন্য আপনাকে আমন্ত্রণ জানানো হচ্ছে।

গবেষণাটির সঙ্গে কি কি জড়িত থাকবে সেইসব তথ্য এই সম্মতির ফরমটিতে আছে। আপনি এটা পড়ুন (বা কেউ আপনাকে তা পড়ে শোনান) এবং তারপরে আপনি এটাতে অংশগ্রহণ করতে ইচ্ছুক কি না সেই ব্যাপারে সিদ্ধান্ত নেওয়া গুরুত্বপূর্ণ। আপনার কোনও প্রশ্ন থাকলে গবেষণা চিকিৎসককে সেই ব্যাপারে প্রশ্ন করতে পারেন।

আপনার চিকিৎসক আপনাকে এই সই বা টিপসই করা ফরমের একটি কপি দিবেন।

গবেষণার উদ্দেশ্য এবং আপনার নিকট থেকে প্রত্যাশাঃ

রোগীর সিটি এনজিওগ্রাফী করা পরীক্ষা চলার সময় কন্ট্রাস্ট ব্যবহার করা হবে। এই কন্ট্রাস্ট ব্যবহার করার ফলে রোগীদের কিডনীর উপর কেমন প্রভাব পড়ে তা আমরা গবেষণা করে দেখব। পরীক্ষার পূর্বে আপনার কিডনীর সেরাম ক্রিয়েটিনিন লেভেল নির্ণয় করা হবে। আপনার পরীক্ষার ৪৮-৭২ ঘন্টার পর আবার আপনার কিডনির সেরাম ক্রিয়েটিনিন লেভেল নির্ণয় করা হবে। এবং ৭ দিন পর আবারও আমরা তা নির্ণয় করব।

আপনার পরীক্ষার পর আপনাকে একটি ফরম দেওয়া হবে। সেখানে আপনার পূর্বের রোগের বিবরণ, আপনার স্বাস্থ্য এবং আপনার জীবনধারা সম্পর্কে জানতে চাওয়া হবে।

আমরা আশা করি আপনি এই ফরমটি পড়ে আমাদের গবেষণাতে অন্তর্ভুক্ত হবেন এবং আপনি আমাদেরকে আপনার তথ্যগুলো দিয়ে সহায়তা করবেন। এই বিষয়ে আপনি সম্পূর্ণ স্বাধীনভাবে সিদ্ধান্ত নিতে পারবেন আপনি গবেষণাতে অন্তর্ভুক্ত হবেন কি না।

তথ্যাবলির ভবিষ্যৎ ব্যবহারঃ

গবেষণাটি থেকে সংগৃহীত তথ্যে ভবিষ্যৎ ব্যবহারের ক্ষেত্রে, আমরা সমস্ত গবেষণা অংশগ্রহণকারীর পরিচিতির গোপনীয়তা বজায় রাখব।

সম্মতিঃ

অংশগ্রহণকারীর নামঃ _____

আম্মাকে গবেষণাটি সম্বন্ধে প্রয়োজনীয় তথ্যাবলী দেওয়া হয়েছে। আমি সম্মতির ফর্মটি পড়েছি, বা আমাকে কেউ সেটা পড়ে শুনিয়েছেন। আমি প্রশ্ন করতে সক্ষম হয়েছিলাম এবং কোনো একজন আমার প্রশ্নগুলির উত্তর দিয়েছেন।

আমি যে কোনো সময়ে চিকিৎসার সুবিধালাভ হারানো ছাড়াই আমার সম্মতি প্রত্যাহার করে নিতে পারি।

আমি ভবিষ্যৎ সংরক্ষণ এবং ব্যবহারের জন্য আমার তথ্যাবলী সংগ্রহের অনুমোদন দিচ্ছিঃ হ্যা না

নিচে আমার সই (বা টিপসই) এটা নির্দেশ করছে যে আমি এই গবেষনাটিতে অংশ নিতে সম্মত আছি।

আমি সম্মত হচ্ছি যে আমার গবেষণাসংক্রান্ত তথ্যাবলী এবং চিকিৎসাসংক্রান্ত রেকর্ডপত্র ভবিষ্যতে শিক্ষামূলক যে কোন পকাশনীতে প্রকাশিত হতে পারে।

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অংশগ্রহণকারীর নাম এবং স্বাক্ষর/বাম বৃদ্ধাঙ্গুলের টিপসই তারিখ

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প্রধান গবেষকের নাম প্রধান গবেষকের স্বাক্ষর তারিখ

Chapter 8

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