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# The Journal of Ad-din women's medical college

## Volume 1, Number 2, December 2013

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- (ii) Materials and methods
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The purpose of the article the rationale for the study or observation should be summarized, only strict pertinent references to be given and data or conclusion from the work being reported not to be included.

#### • Material and methods

In this section selection of the observational or experimental subject (patient or laboratory animals, including control) should be described clearly. The age, sex and other characteristics of the subjects should be identified. Identify the methods, apparatus, and procedure in sufficient detail to allow other worker to reproduce the result. Give references to establish methods, including statistical methods. Precisely identify all drugs and chemicals used, including generic name, dose and route of administration. Author submitting review manuscripts are advised to include a section describing the methods used for locating, selecting, extracting and synthesizing data.

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## Editorial

### 'Prostate the Silent Killer'

As lifespan is increasing, the geriatric health problems are also increasing throughout the world. Prostate is an important glandular organ of male genital system. It is situated at the junction of urethra and urinary bladder. It plays very important role in male sex. It contributes fluid in semen and helps in maturation of sperm. The gland begins to increase in size at the age of 30 onwards. As we know, with the advancement of age, the vision become poor, the hair becomes gray, the skin becomes wrinkled, same way the prostate gland increases in size. Only increases in size is not a big problem. But due to enlargement, if flow of urine is obstructed, then it creates a great problem, which needs to be addressed immediately. Obstruction of flow of urine or any other difficulties in relation to voiding can be easily diagnosed and properly managed either medically or surgically.

The most alarming news for elderly male is that prostate is the place where malignancy can grow, develop and spread to different parts of the body even without knowledge of the person and producing any voiding problem. In other words, prostate can harbor cancer even up to death limit without knowledge of the individual. That's why prostate is called the 'silent killer'.

Prostate can be compared with the breast of female. Like prostate breast is also a glandular structure where malignancy can grow. But, as breast can be self examined and easily palpable, signs are easily identified which is totally reverse in case of prostate gland. In one study it has been shown that the chance of having prostate cancer in 90 years old male is 90%. Breast screening is well established procedure for early detection of breast cancer and management. The terminology is not that much new to our physician and the common people, whereas care of

prostatic health or prostate screening is not well known to all. It is the time to make awareness among the doctor's community as well as common people. No doubt the screening program is costly but the community has got the fundamental right to know the importance of the program and consequence of negligence. At least there should be the adequate dissemination of information among the public, so that, the liabilities do not come on the shoulders of medical professionals. Establishment of prostate screening program of the whole nation is costly but the consequence of ignorance should be communicated to the public either through print or electronic media.

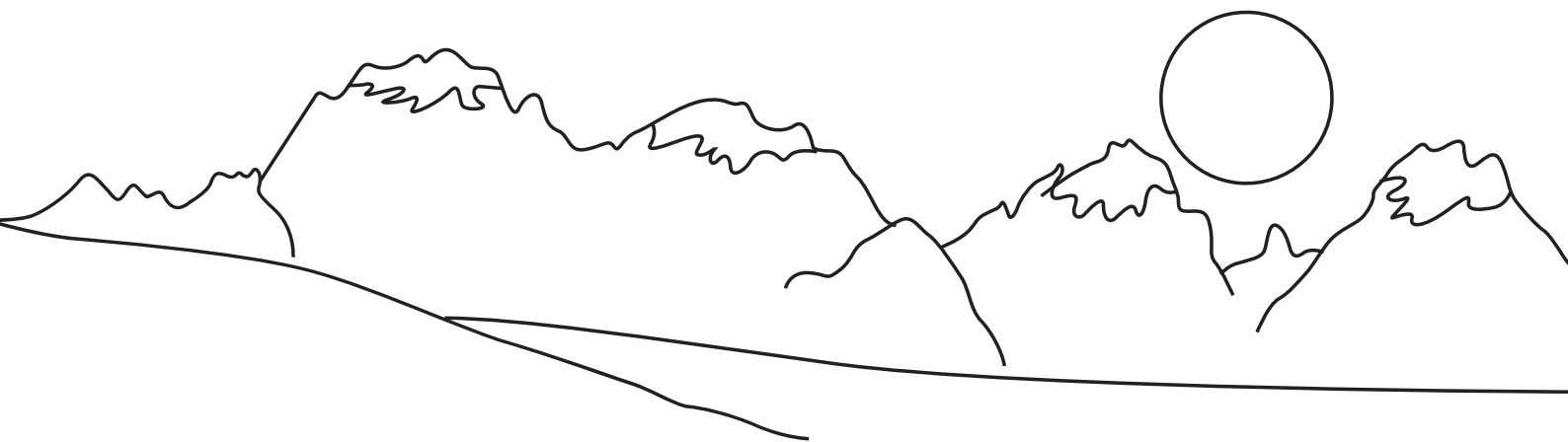
In a limited study in a rural area of Bangladesh it has been found that 39.5% of elderly male suffer from symptomatic prostate and 10% of them need surgical intervention and 12% of operated cases showed different types of malignancy. Although the nation-wide survey has not yet been done, it appears from the studies conducted by different agencies that the incidence of prostate cancer in elderly male in our country is quite alarming compared to the western world.

In Asian countries like Singapore they are trying to fix a particular week of a year as 'Prostate Day' or Prostate Week to increase the public awareness regarding the gravity of the problem. In our country, we also sporadically tried but it needs systematic and well-organized campaign to make our people aware of this deadly disease.

In advanced world the population of elderly male is more, as well as geriatric health problems like prostate related problems are also a big issue. In public places in Australia specially public wash room areas small wall writings

mentioning symptoms of prostate related diseases are commonly seen. These could increase public awareness about the prostate cancer which is a life threatening disease. We should think about the issue and focus light on it for public interest.

Prof. Dr. Afiquor Rahman  
Professor of Urology, AWMC



*We grow through your faith*

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## Original Articles

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## Original Article

# Coagulation Profile Assessment and its application in Preparation of Laparoscopic Surgery

Mahamud Riyad<sup>1</sup> Md. Shihab Uddin<sup>2</sup>

### Abstract

**Objective :** To assess the usefulness of practicing preoperative coagulations tests in preparation of laparoscopic surgical procedures.

**Design :** Retrospective observational study.

**Setting :** King Fahad Medical City a tertiary-care referral center in Saudi Arabia.

**Methods :** Five hundred and fifty adult patients scheduled for elective laparoscopic surgery were studied to determine whether plan of management was influenced by routinely done Bleeding time, Platelet count, Prothrombin time, Activated Partial Thromboplastin time and International normalization ratio.

**Results :** No intervention or change of management was identified in 463 patients whom coagulation profiles were done routinely as part of pre-operative preparation. However, management plan was changed in 5 (5.75%) of 87 patients having indications for coagulation profile test ( $P < .01$ ).

**Conclusion :** The study shows that preoperative screening tests for coagulopathies not suspected on the basis of detailed clinical information are unnecessary and should not be done.

**Key Words :** Coagulation profile, indication, screening test, indicated test, intervention.

### Introduction

Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), International Normalization Ratio (INR), Platelet Count (PC) and Bleeding Time (BT) are commonly ordered by clinicians as part of preoperative assessment. In preparation of patient for laparoscopic procedure these tests are never missed in KSA and some other countries like India. In Bangladesh though coagulation profile is not mandatory for all patients but still it is widely practiced by the surgeons and anesthesiologists before laparoscopic procedure.

Evidence based guidelines on the use of pre-operative tests before elective surgery have been published by the National Institute for Clinical Excellence (NICE) a government organization in the UK in 2003 where these tests were not recommended routinely either in adult or in children before elective procedure in the absence of positive family or personal history of bleeding disorder<sup>1</sup>. More recently British Committee for Standards in Haematology has confirmed the NICE guidelines appropriateness regarding this<sup>2</sup>.

American Society of Anesthesiologist (ASA) has published an advisory in 2002 saying that patient with negative abnormal bleeding history does not require coagulation screening prior to surgery<sup>3</sup>. A prospective study showed proper history taking can safely and effectively supplement preoperative screening test for coagulopathy<sup>4</sup>. British Committee for Standards in Haematology also stated that unnecessary testing can delay surgery in appropriately

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because of low positive predictive value of these tests<sup>2</sup>. Canadian Anesthesiologist Society (CAS) published a simple guidelines regarding routine preoperative coagulation test<sup>5</sup>. In a systemic review done in Johns Hopkins University School of Medicine in 2005 conclude that there is very insufficient evidence to conclude that abnormal test results predict per operative bleeding and suggested RCT to provide strong evidence<sup>6</sup>. On the other hand Italian Society for Haemostasis and thrombosis recommended that PT, PTT, INR should be performed routinely before any invasive or surgical procedure<sup>7</sup>. There are many other studies and case reports supporting preoperative some sorts of coagulation profile<sup>8,9</sup>. Most of the country in Europe follows NICE guidelines and some other country is trying to prove this thought in their population for specific operations. For instance, coagulation status is routinely checked before any operative procedure in Germany but German Society for Ear-Nose-Throat-Medicine, Head and Neck Surgery (DGHNO), the Working Group Paediatric Anaesthesiology of the German Society of Anaesthesiology and Intensive Care Medicine (DGAI), the German Society of Paediatric Medicine (DGKJ), and the Paediatric Committee of the German Society of Thrombosis and Haemostasis Research (GTH), published in the *Deutsches Ärzte blatt* in 2006, stressed that coagulation screening is not useful in the preoperative setting and advised to draw more attention on the patient's detailed history<sup>10</sup>.

It is obvious that preoperative routine coagulation profile is still in practice and a matter of contention between the physicians. In most of the country it is considered as an obligatory part of preoperative evaluation for laparoscopic surgery. One of the reasons behind that is surgeon is very much cautious about bleeding during laparoscopic procedures, others are more general, to-detect unsuspected abnormalities that might influence the risk of operative morbidity and mortality; establishing a baseline value for a test that has a likelihood of being monitored and changing after the surgical procedure; for medico-legal reasons; and as a tradition in individual institutional practices.

Here in Saudi Arabia we found that no patients undergo elective surgical procedures without coagulation testing. In our institution, a tertiary referral hospital in the capital drawing a general catchment from all over the country PT, PTT, INR, BT & PC are a routine practice for all elective surgical patients. Since it is already proven that routine preoperative investigations is not necessary by the major medical societies of the world, we decided to check if

there is any role of coagulation profile in preparation of patient for laparoscopy surgery.

## Methodology

### Study Design : Retrospective chart review

**Place Of Study :** Department of Surgical Specialties, King Fahad Medical City, a tertiary care super specialized referral center, Riyadh, Saudi Arabia.

## Methods

Upon approval from IRB (Institutional Review Board) all patients underwent Elective Laparoscopy Surgery in the year 2009 was identified from Operation Theater and Anesthesia Department co-ordinated data base system. We excluded pediatric patients, emergency procedures and pregnant patients. Elective surgery was defined as scheduled operation list published and distributed day before surgery.

To identify patients predisposed to an abnormal coagulation system, a comprehensive list of indications (Table 1) for pre-operative coagulation testing was derived with guidance of CAS (Canadian Anesthesiologist Society) guidelines, ASA (American Society of Anesthesiology) advisory and Harvard medical school study<sup>11</sup>. Based upon the listed questionnaire patients file was reviewed to divide them into "Indicated Test Group" and "Screening Test Group". Indicated Test Group patients were those whom coagulation test results might had been abnormal due to specific findings in history and physical examination. Screening Tests Group Patients were those whom these investigations were not specifically needed therefore, were done as screening for an unsuspected coagulopathy.

Preoperative INR, PT, PTT, BT & PC results recorded from hospital electronic data base system. Post-operative results (up-to 28 days post-op period) also searched and recorded when available. Any change of management plan to overcome the abnormal results termed as "Intervention", was identified from physician order documented in the file. Cancellation of procedure, transfusion of Packed RBC, whole blood in excess of normal due to coagulopathy, transfusion of fresh frozen plasma, platelets, or other coagulation factors and Vit K injection were taken as intervention whereas preparation of packed RBC or total blood in an operative procedure where generally not ordered is also considered as change of management. Pre-operative blood transfusion for anemia or blood transfusion for major surgery in absence

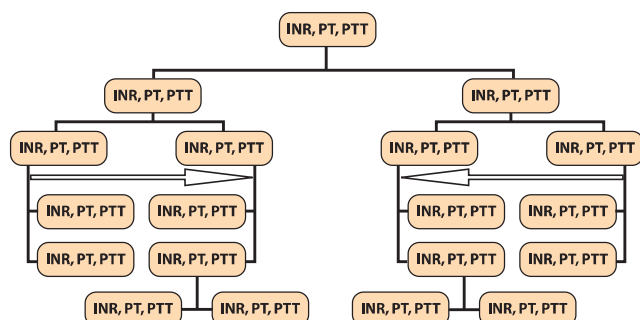


of positive bleeding history was not considered as interventions for coagulation profile tests.

## Results

Statistical comparisons between the two groups in context of required interventions were made using Fisher's exact test, with the level of significance taken as  $p < 0.05$ .

**Figure 1 :** Study scheme showing group differentiation.



**Table 1 :** Indications to request preoperative coagulation profile

• Bleeding diathesis,	
• Family history of bleeding disorder	Prolonged bleeding Excessive bleeding Easy bruising Unable to give history
• Anticoagulant therapy	Aspirin Heparin, Enoxaparine Dipyridamol Warfarin Nonsteroidal anti-inflammatory drugs
• Past Medical History	History of deep venous thrombosis or pulmonary embolism. Chronic renal failure on dialysis Cirrhosis, jaundice Splenic disease Platelet dysfunction Thrombocytopenia
• Malignancy	Metastatic carcinoma Malignancy with radio-chemotherapy
• Physical Examinations	Petechiae Echymosis Jaundice Hepatomegaly, nodular liver Ascitis Splenomegaly

**Table 2 :** Demographic Data and Distribution of Patients

Patients (n)	Number	Percentage
Total	550	100%
Male	89	16.18%
Female	461	83.82%
General Surgery	301	54.72%
Gynecology	224	40.73%
Urology	25	04.55%

**Table 3 :** Laparoscopic procedures performed

Name	Number	Percentage
Laparoscopic Cholecystectomy	245	44.55%
Laparoscopic Ovarian cystectomy/ Ophorectomy/ salphingo-ophorectomy	63	11.46%
Total laparoscopic hysterectomy and laparoscopy assisted vaginal hysterectomy	62	11.27%
Diagnostic laparoscopy with or without hysteroscopy	46	8.36%
Laparoscopic myomectomy	29	5.27%
Laparoscopic Sleeve gastrectomy	23	4.18%
Laparoscopic Colorectal procedures	20	3.64%
Laparoscopic pancreatectomy, spleenectomy, adrenalectomy, Nephrectomy	17	3.09%
Laparoscopic vericocelectomy	13	2.36%
Others	32	5.82%
Total	550	100%

A total 550 adult patient underwent elective laparoscopic surgery, of them 461(83.82%) patients was female (table 2). Laparoscopic cholecystectomy (table 3) was the commonest procedure 245 (44.55%).

Among the 87 patients whom the coagulation profile was indicated, 14 (16.09%) patients had abnormal results, requiring intervention preoperatively for 5(5.75%) patients (Table 4), 463 patients were in the Screening Test group. Of those, 455 (98.27%) patients were found to have normal results. Even the 8 (1.73%) patients with abnormal results didn't require any intervention. The difference in the change of management (Table 4) between the two groups were highly significant ( $P<.01$ ).

**Table 4 :** Summary of the coagulation profile results (P<0.01)

Test Indicated			Screening Test		
Normal	Total Abnormal	Abnormal with Intervention	Total	Normal Abnormal	Abnormal with Intervention
73	14	5	455	8	0
83.91 % 16.09%		5.75% (35.71%)*	98.27%	1.73%	-
Total number of patient = 87 (15.82%)			Total number of patient = 463 (84.18%)		

\*35.71% of abnormal results (5 of 14) needed intervention  
which were 5.75% of total (5 of 87)

Among the test indicated group test was repeated at least once or multiple times in 45 patients (Table 5). 9 patients had once or more than once abnormal results and interventions were needed in 4 patients. On the other hand, 113 patients of the screening group were found to have coagulation profile repeated within 28 days post-operative period, only 3 patients had abnormal results, again not needing any active management.

**Table 5 :** Available post-operative coagulation profile results ( $P < 0.01$ )

Test Indicated Group			Screening Test Group		
Normal	Total Abnormal	Abnormal with Intervention	Normal	Total Abnormal	Abnormal with Intervention
36	9	4	110	3	0
Total number of patient = 45			Total number of patient = 113		

## Discussion

The current study is the first ever evaluation regarding the usefulness of routine preoperative coagulation testing in case of only laparoscopic surgery patients. Comprehensive criteria derived from the patient history and physical examinations were used to determine that preoperative coagulation testing was indicated or not. The questionnaire was designed to supplement the standard history and physical examination by the chart reviewing physicians. It was made by assistance of a number of strong international guidelines CAS, ASA and Harvard medical school study to keep the evaluation process simple and which can be a tool for the surgeon and anesthetist for pre-operative assessment of patient in future. When these criteria were applied to the general, gynecological and urological elective surgery patients who had been operated laparoscopically, 87 (15.82%) of them had at least one indication for the test. In 84.18% (463) of the patient test were not indicated were truly screening tests for an occult coagulopathy because they could not have been otherwise suspected. Although 1.73% of the screening tests were abnormal, all ignored by the surgeon and anesthetist, because they were marginally prolonged. Literature also suggests that minimally deranged coagulation result have a poor predictive value for a surgically significant coagulopathy<sup>12</sup>. Following an abnormal test result clinicians may go for correction of it, whereas a serious abnormality may suggest the surgery to be cancelled or delayed. But commonly most abnormalities are simply ignored. Roizen MF et al ignore more than 60% of abnormalities discovered on routine preoperative tests<sup>13</sup>. In our patients, 35.71% of abnormal results in indicated test group were taken for active management by the physicians others were simply ignored, whereas all<sup>8</sup> the abnormal results were amenable to overlook in screening test group.

Post operatively (up to 28 days), some patients with major surgery and had to stay in hospital for couple of days, found to have repeat coagulation profile. There was no intervention identified in screening test group in comparison to 4 interventions in patients of indicated test group. We did not put emphasis on these findings in our study as all the patient had not gone through the same investigations after operation, although it gave an idea

that illogical coagulation profile has no role in laparoscopic surgical procedures even in post-operative period.

Our study is retrospective; our control and study groups were not matched in number, age and sex, which could have influenced our test of significance. Most of our patients are female 461(83.82%) this was because gynaecological laparoscopic procedures 224(40.73%) were included in the study. Moreover, our single most performed surgery was Laparoscopic Cholecystectomy which was also overtly dominated by female. We found a relatively high number of abnormal results in the screening test groups because we followed our local hospital definitions of abnormal results, rather than the more practical "action limits". We also considered total test result as abnormal when any component of the test breached the reference value. For instance, we labeled total coagulation profile as abnormal when any one of PT, APTT, INR, BT or PC being abnormal, As such, very few actual interventions were needed for these abnormal results. We considered the change of management plan named as intervention to differentiate between the results of two groups, as minor change of test value has no real benefits to calculate. Test values also fluctuate by reagent used and analyzer machines.

In summery, we couldn't appreciate any special clue or danger to carry on with the same traditional practice of routine pre-operative coagulation tests for laparoscopic procedures. The results of our study show that most tests 84.18% (463, Table 4) ordered at our institution are incompatible with the applicable published guidelines. To follow established guidelines is usually the exception and not the rule in the majority of health institutions in the World. This failure to convert recommendations into practice is often not related to the content or quality of the guidelines themselves but is more related to difficulty changing established behavior of clinicians and institutions in addition to failure of dissemination, cost, and doubt of guideline's applicability in local populations<sup>14</sup>. We hope that our study result will be a guideline for asking coagulation profile tests in KSA as well as Bangladesh which will reduce the un-necessary financial burden on the society and patients.

## Conclusion

It can be suggested based on our findings that routine preoperative PT, APTT, INR, BT, PC can be safely eliminated from preparation of patient for laparoscopic procedures by careful history taking and clinical examinations without endangering patient's life or adversely affecting the outcome.

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## Original article

# Comparative effect of Nigella sativa, Aspirin & Hydrocortisone on chronic inflammation

Saima Parveen<sup>1</sup>, Moniruzzaman Bhuiya<sup>2</sup>

### Abstract

**Objective :** Evaluation the anti-inflammatory effects of Nigella sativa on the cotton pellet induced inflammation in rats and to compare the effects of ethanol extract of Nigella sativa with aspirin and Hydrocortisone. Nigella sativa Linn (Family: Ranunculaceae) is a common spice of south east asia especially in Bangladesh and locally called Kalajira.

**Year of Study :** January 2008 to December 2008.

**Methods :** Chronic inflammation was induced by subcutaneous implantation of a sterile cotton pellet in rat's groin region. The experiments was designed to demonstrate the anti-inflammatory effects of different doses of Nigella sativa extracts and to compare the effects with that of available anti-inflammatory drugs i.e. Aspirin and Hydrocortisone as reference standards for 14 days.

**Result :** The effect was compared with reference standard drugs aspirin and hydrocortisone. Treatment with Nigella sativa extract at a dose of 250mg/kg body weight and at a dose of 500mg/kg body weight orally daily for 14 days produced anti-inflammatory effect. And the percentages of inhibition of granuloma formation were 19.3% and 41.42% respectively. Following administration of aspirin and hydrocortisone for 14 days, showed also anti-inflammatory effect and the percentage of inhibition of granuloma formation were 27.67% and 38.58% respectively.

**Conclusion :** The obtained data support the basis for future use of Nigella sativa in reducing morbidity and mortality resulting from inflammatory disease condition.

**Key words :** Chronic inflammation, Nigella sativa, Aspirin , Hydrocortisone.

### Introduction :

Inflammation is the result of our body's response to an injury or an infection, in other word it is a defense mechanism. Unfortunately, this protective response of our immune system can result in damage to our body's organ<sup>1</sup>.

Globally the average lifespan has increased the incidence of communicable and non-communicable diseases chronic and degenerative diseases such as cardiovascular diseases, cancer and rheumatic diseases are most common and significant causes of disability and mortality and carry a high socio-economic cost. Rheumatoid disease is one of the commonest chronic inflammatory condition and affect people of both sexes of all ethnic groups and ages. Rheumatoid arthritis has a world-wide distribution and affects 0.5-3% of the population and leads to chronic inflammation, granuloma formation and joint

destruction. Diseases of inflammation and immunity can occur when the normal inflammatory response progresses to chronic inflammation either because of long term inappropriate response to a stimulus or because the offending agent is not removed for example chronic infection, transplantation and autoimmunity<sup>2</sup>. To relieve those conditions various steroidal and non-steroidal drugs are used. Prolonged uses of both steroidal & non-steroidal anti-inflammatory drugs are well known to be associated with peptic ulcer formation. Hence, search for new anti-inflammatory agents that can retain therapeutic efficacy & yet are devoid of these adverse effects is justified. There is much hope of finding active anti-rheumatic compounds from indigenous plants as they are still used in therapeutics despite the progress in conventional chemistry and pharmacology in producing effective drugs. Traditional use of kalajira as a poultice of ground seeds for inflammatory ailments such as rheumatism, use of herbal medicine throughout the world is increasing. Plants still remaining the primary source of supply of many important drugs used in modern medicine. Therefore, studies are still going on in search of more potent, less toxic, cheaper and easily available anti-inflammatory agents. To treat these inflammatory

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conditions medications are used, but medications can have side effects. However herbal medications usually are devoid of such problems. For this reason the present study was selected to evaluate the anti-inflammatory activity of *Nigella sativa* in experimentally induced inflammation in rats. *Nigella sativa* Linn (Family: Ranunculaceae) is a common spice of south East Asia especially in Bangladesh and locally called Kalajira. The plant enjoys vast folklore uses as traditional medicine. The *Nigella sativa* that is kalajira is healing for all diseases except death<sup>3</sup>. *Nigella sativa* has been in use in India and many Middle Eastern communities as natural remedy of many acute and chronic conditions for two thousand years, traditional use of kalajira as a poultice of ground seeds for inflammatory ailments such as rheumatism. Kalajira as a poultice of ground seeds for inflammatory ailments such as rheumatism, headache and certain skin conditions is supported by modern studies. The seeds are used for inflammatory actions. Thymoquinone an active constituent of kalajira is a potent inhibitor of thromboxane  $B_2$  and leukotriene  $B_2$  through the inhibition of cyclooxygenase and lipoxygenase respectively<sup>4</sup>. Proper scientific investigation of the properties of ground seed may substitute the presently available anti-inflammatory agents and thereby establish its position in modern medicine as more safe, efficacious and cost effective drug. The present study has aimed at a view to explore the possible anti-inflammatory properties of *Nigella sativa* Linn. For this reason the present study was selected to evaluate the anti-inflammatory activity of *Nigella sativa* in experimentally induced inflammation in rat. As our knowledge goes no other work has been done on the chronic anti-inflammatory effect of *Nigella sativa* or kalajira in our country. Considering its medicinal value and availability in our country this study was undertaken to evaluate the anti-inflammatory effect of the ground seed of *Nigella sativa* in rat models. In this study of chronic inflammation were tested and anti-inflammatory effects of *Nigella sativa* were compared with both steroidal and non steroidal anti-inflammatory agents.

Our objective of study was to induce chronic inflammation by subcutaneous implantation of cotton pellet, to use two doses of ethanol extract of ground seed of *Nigella sativa* in carrageenin and cotton pellet induced inflammation in rats, to measure dry weight of granuloma, to compare the effects of ethanol extract of *Nigella sativa* with Aspirin and Hydrocortisone.

### Materials and method

The ground seed of *Nigella sativa* was collected from

National Herbarium and was taxonomically identified by Department of Botany, University of Dhaka. After collection crude ethanol extract was formed and kept in 4°C in refrigerator. Long Evans Norwegian rats, collected from BSMMU (3-4 months old, 200-250gm of weight), had free access of food and water and libitum. Chronic inflammation was induced by cotton pellet. The anti inflammatory effect was compared with reference standard drugs aspirin and hydrocortisone.

### Method

The rats used in this method were divided into five group (n=6), fasted overnight and allowed free access to water. The rats were administered with vehicle, standard drug and test drugs. One hour after the first dosing, the rats were anesthetized with ether<sup>5</sup> and 50mg of the sterile cotton pellet was inserted one in each axilla and groin of rats by making small subcutaneous incision. The incisions were sutured by sterile catgut (Crunkhon et al., 1971)

Group-I: Received 0.6 ml normal saline administered orally for 14 days and served as control.

Group-II: Received Ethanol extract of *Nigella sativa* 250mg/kg body weight administered orally for 14 days.

Group-III: Received Ethanol extract of *Nigella sativa* 500mg/kg body weight administered orally for 14 days.

Group-IV: Received Aspirin 100mg/kg body weight administered orally for 14 days.

Group-V: Received Hydrocortisone 2mg/kg body weight administered subcutaneously for 14 days.

The animals were sacrificed by excess anesthesia on the 14<sup>th</sup> day and cotton pellet are removed surgically. Pellets are separated from extraneous tissue and dried at 60°C unit weight become constant. The net dry weight i.e. after subtracting the initial weight of the cotton pellet was determined. The average weight of the pellet of the control group as well as of the test groups was calculated. The percent change of the granuloma weight relatively with vehicle control was determined and statistically evaluated. The percentage inhibition increases in the weight of the cotton pellet is calculated.

All the results were expressed as mean  $\pm$  s.e.m. Significance of difference between groups was assessed by using student's 't' test.

### Results

At the end of the chronic anti-inflammatory study after 14 days the pellets were removed from the site of insertion sacrificing the animals<sup>6</sup>. The final weight of the cotton

pellets were determined. The weights were  $207.83 \pm 0.69$ mg,  $177.63 \pm 5.31$ mg,  $142.45 \pm 5.58$ mg,  $164.16 \pm 15.86$ mg,  $146.93 \pm 7.12$  mg for group-I, II, III, IV and V respectively. The increment in the weight of cotton pellet in ethanol extract of *Nigella sativa* 250mg/kg body weight, ethanol extract of *Nigella sativa* 500mg/kg body weight, aspirin and hydrocortisone treated groups were  $127.63 \pm 5.31$ ,  $92.45 \pm 5.58$ ,  $114.16 \pm 15.86$ ,  $96.93 \pm 7.12$ mg respectively. Whereas, the increment of the pellet for the control group was  $157.83 \pm 8.69$  mg. The percentage of inhibition of granuloma formation were 19.13, 41.42, 27.67, 38.58 as compared to the control for in ethanol extract of *Nigella sativa* 250mg/kg, ethanol extract of *Nigella sativa* 500mg/kg, aspirin 100mg/kg and hydrocortisone 2mg/kg body weight respectively. In this chronic study an anti-inflammatory effect was observed at 500mg/kg body of the ethanolic extract of *Nigella sativa*.

**Table I :** Effects of extracts of *Nigella sativa*, Aspirin and Hydrocortisone on cotton pellet induced granuloma in rat.

Groups	Initial weight of cotton pellet (mg) (MEAN $\pm$ SEM)	Final weight of cotton pellet (mg) (MEAN $\pm$ SEM)	Increase of weight of cotton pellet (mg) (Mean $\pm$ SEM)	Inhibition of granuloma formation %
Group I	50 $\pm$ 0.22	207.83 $\pm$ 0.69	157.83 $\pm$ 8.69	—
Group II	50 $\pm$ 0.22	177.63 $\pm$ 5.31	127.63 $\pm$ 5.31*	19.13
Group III	50 $\pm$ 0.22	142.45 $\pm$ 5.58	92.45 $\pm$ 5.58**	41.42
Group IV	50 $\pm$ 0.22	164.16 $\pm$ 15.86	114.16 $\pm$ 15.86**	27.67
Group V	50 $\pm$ 0.22	146.93 $\pm$ 7.12	96.93 $\pm$ 7.12**	38.58

\* P<0.05 in a test of significance difference from control.

\*\* P<0.001 in a test of significance difference from control

## Discussion

Treatment with *Nigella sativa* extract at doses of 250mg/kg body weight orally daily for 14 days produced significant anti-inflammatory effect and at a doses of 500mg/kg body weight orally daily for 14 days produced significant anti-inflammatory effect and the percentage of inhibition of granuloma formation were 19.30% and 41.42% respectively. This was also in a dose dependent manner. Following administration of aspirin and hydrocortisone for 14 days showed also anti-inflammatory effect and the percentage of inhibition of granuloma formation were 27.67% and 38.58% respectively.

In the cotton pellet granuloma model, inflammation and granuloma develops during the period of several days. This model is an indication for the proliferative phase of inflammation. Inflammation involves proliferation of macrophages, neutrophils and fibroblasts, which were basic sources of granuloma formation. Hence, the decrease in the weight of granuloma indicates that the

proliferative phase was effectively suppressed by the ethanol extract of *Nigella sativa*.

The anti-inflammatory effect produced by *Nigella sativa* in response to cotton pellet induced granuloma formation was most likely to be mediated through prostaglandins (PGs). This was supported by the fact that aspirin, an inhibitor of PGs synthesis<sup>7</sup> produced similar results. Furthermore, *Nigella sativa* produced anti-inflammatory effect comparable to hydrocortisone indicating that it may also act by stabilizing the lysosomal membrane.

*Nigella sativa* reduced the vascular component of inflammation and impaired the release or formation of inflammatory mediators such as PGs, histamine, leucotrienes etc. responsible for increasing vascular permeability and inflammation. It may also inhibited the amoeboid activity of the reticuloendothelial cells and polymorphonuclear leucocytes resulting a reduction in the cellular exudates<sup>8</sup>.

In this study, crude ethanol extracts of ground seed of *Nigella sativa* steroidal and non-steroidal anti-inflammatory drugs daily for 14 days and reduced weight of granulation tissue. The reduction was statistically significant in comparison to control group which was observed at the higher doses (500mg/kg body weight). But the reductions of weight of granulation tissue in case of steroidal and non-steroidal anti-inflammatory drugs were highly significant in comparison to ethanol extract of ground seed of *Nigella sativa*.

Further investigations were warranted to reconfirm and identify the anti-inflammatory active principles and elucidate their mechanism of action. Toxicological studies should also be under taken before any clinical use.

The study was basically pharmacological one and both the modern drugs and herbal products were used to influence the biological system. It was evident that the biological systems have certain limitations, like individual variations, interference in the response with the system, variability in methods and other factors, which might have interfered with primary findings. However, the results obtained in this experiment may not represent the exact effect. Despite all these limitations, interpretation of the results obtained in this study was made carefully and cautiously.

## Conclusion

The study provides an initial step on demonstrating the anti-inflammatory effect of ethanol extract of ground seed of *Nigella sativa* in anti-inflammatory state. The obtained data support the basis for future use of *Nigella sativa* in traditional system of medicine. Thus, it could be a new

agent in reducing morbidity and mortality resulting from inflammatory disease condition. The findings presented here provide a baseline for future studies designed to quantify the effects of ethanol extract of ground seed of *Nigella sativa*. The experimental results suggest that the possible mechanism of anti-inflammatory activity of polyamines may be due to their impairment of the release or formation of inflammatory mediators such as histamine, 5-HT, PGs, and lysosomal membrane stabilization as supported by our experimental findings. Studies on polyamines may be helpful in developing a new approach for better understanding of the inflammatory process and the generation of new anti-inflammatory drugs.

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## Original Article

# Variation of index (2D) and ring (4D) digit lengths and their ratio (2D:4D) among adult females of Bangladesh

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### Abstract

**Objective :** In Human hand. by virtue of evolution and genetically arrangements, digital lengths vary from person to person according to age, sex, races, occupation or even environmental influences. It has been found that the digital lengths and their ratios are not the same in different sexes or even both hands. Specially, index to ring digit lengths and their ratios which already have been proved to represent sexual dimorphism may differ in both hands of an individual. In this study, this variation of the index finger (2D) and ring finger (4D) length and their ratio (2D:4D) has been analyzed and compared in both hands among the adult females of Bangladesh.

**Materials & Methods :** A Cross sectional analytical study was conducted in the department of Anatomy, Dhaka Medical College, Dhaka, from July 2012 to June 2013. The study was performed on 100 female MBBS students (20-25 years of age) of Dhaka Medical College, Dhaka. With the help of digital vernier caliper measurements of digital lengths were recorded. Paired t- test was done for statistical analysis of the results.

**Results :** There was no significant difference between the lengths of right (R2D) and left (L2D) index finger but the length of right ring finger (R4D) was significantly greater ( $P < 0.001$ ) than left ring finger (L4D). The right index to ring digit ratio (R2D:4D) was significantly less than left index to ring digit ratio (L2D:4D) in female ( $P < 0.001$ ). Also, right index to ring digit ratio (R2D:4D) was recorded  $< 1.00$  in 36% and  $\geq 1$  in 64% subjects and left index to ring digit ratio (L2D:4D) was recorded  $< 1.00$  in 07% and  $\geq 1$  in 93% of subjects. This indicates sexual dimorphism in 2D:4D ratio is more prominent in the left hand of female.

**Conclusion :** Digital lengths especially index (2D) and ring (4D) digit lengths are often use to determine sexual dimorphism. Also, study over the variations of digital lengths have great medicolegal importance to determine age, sex and race of an individual.

**Keywords :** Index finger length (2D), ring finger length (4D), index to ring finger ratio (2D:4D)

### Introduction

It has been known for a long time that any measurements of body parts can change with the alterations in size of the organs involved or general body size and this concept was defined concisely by Levinton<sup>1</sup>. Throughout the following decades, many studies have been conducted regarding body anthropometry and sexual variations. One such study is has gained marked interest in medical science that is measurement of digital lengths and their sexual variations. The index finger located between thumb and middle finger is the second digit (2D) and ring finger is located between middle and little finger are two

most dexterous and sensitive fingers of a human hand<sup>2</sup>. Researchers claimed that the relative lengths of digits are set before birth<sup>3</sup> and they remain unchanged rest of the life. Interestingly, in human hands, the relative lengths of the index finger and ring finger differ between two hands and even between male and female<sup>3</sup>. More recently, the researchers explored the relationship between the index to ring digit ratio (2D:4D) which has been found more practical applications. Many studies among different races have shown that index to ring digit ratio (2D:4D)  $\geq 1$  among female and  $< 1.00$  among male<sup>4</sup>. A wide variety of sex-dependent human behaviors are associated with 2D:4D ratios that has been stated by Manning J.T. & Fink B.5 and those characteristics includes personality traits like dominance, aggression, reproductive success and sexual performance, sexual orientation, hand preference, verbal skills, different physical and mental health issues, or even musical and sporting talents. These associations appear to be often stronger for the right hand<sup>6</sup>. In the study of Manning<sup>7</sup>, it is seen that smaller index fingers in

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women have been associated with higher levels of physical aggression throughout their life<sup>8</sup>. Women with less smaller index finger are reported as being more masculine and dominant in nature and tend to perform better in a number of physical activities<sup>9</sup>. It has been also reported that a number of physical and behavioral traits significantly depends on index (2D) and ring (4D) finger in both sexes. For example, males with smaller index finger and larger ring finger are more fertile and have high life time reproductive success. Also, they are more aggressive and assertive in nature and have high musical and sports aptitudes<sup>10</sup>. Again, male with excessive smaller index finger often has some attributes like left-handedness, good visuo-spatial ability<sup>11</sup>, fast running speed<sup>12</sup> but they may also experience some severe health related problems like autism, Asperger's syndrome, prostatic carcinoma, Hepatitis-B related hepatocellular carcinoma, urolithiasis and rheumatoid arthritis but male having longer index finger often has higher risk of early heart disease<sup>11</sup>. On the other hand, females with long index finger are more fertile, have high reproductive success but also having higher risk of breast cancer and endometrial cancer. Again, female with an excess long index finger are associated with good verbal fluency but higher risk to have neurodegenerative disorders. It has been also reported that females with excessive small index finger with relatively large ring finger have greater tendency towards the homosexuality or bisexuality, spontaneous abortion, polycystic ovaries and also they are more aggressive and assertive in nature<sup>10</sup>. The ratio between the length of the index and ring digit (2D:4D) of an individual found to be correlated with the prenatal testosterone and estrogen levels<sup>4</sup>. There is evidence that a low 2D:4D been positively related to prenatal testosterone while a high 2D:4D is positively associated with prenatal estrogen exposure or in other word a low 2D:4D ratio has been shown to correlate with high testosterone levels which is characteristic of males while a high 2D:4D ratio is correlated with low testosterone level, a characteristic of females. Initially, some other studies have reported null findings regarding these correlation studies and challenge the relationship between 2D:4D and its sensitivity to androgen but in 2009, some experimental studies proved that enhancement of prenatal testosterone reduces 2D:4D and nullify all the challenges.<sup>12</sup>

## Materials & Methods

The study was performed on one hundred (100) female medical students of Dhaka Medical College, Dhaka age ranging from 20-25 years. With the help of a digital vernier caliper the right index (2D) and ring (4D) finger lengths were recorded in centimeters. As ring finger has two creases, the most proximal crease has been chosen. Length was recorded by measuring the crease-tip (c-t) length where "c" is the midpoint of crease at the base of the finger and "t" is extreme end (tip) of the finger that is furthest from the crease. The distance between these two points indicates the length of index (2D) or ring (4D) finger. Measurements were taken three times independently and the maximum length was taken for analysis. Procedure of measurement of index finger (2D) and ring finger (4D) is shown in Fig:-1. The index to ring digit ratio (2D:4D) was calculated by dividing the index finger length with ring finger length. Data was expressed as mean  $\pm$  Standard deviation ( $\pm$ SD) as descriptive statistics. Paired Student's t-test was done to analyze the differences between lengths of right index finger (2D) and ring finger (4D) and their ratios among both hands of female. Statistical significance was accepted at ( $P < 0.05$ ). This thesis work approved by the Ethical Review Committee (ERC) of Dhaka Medical College, Dhaka.

## Results

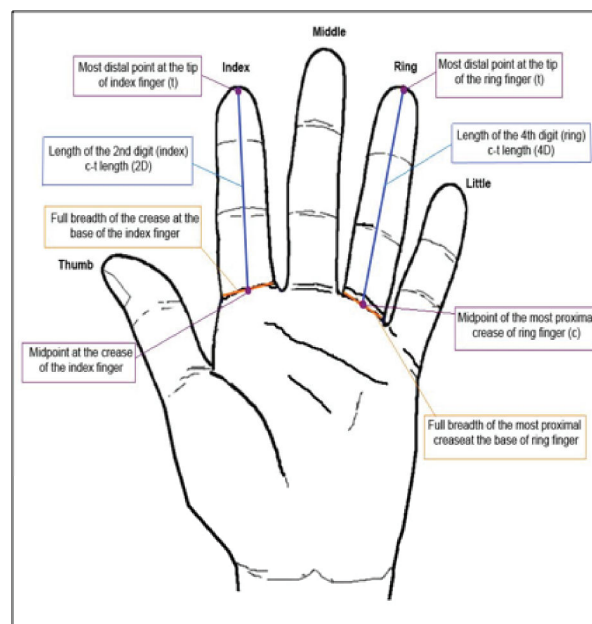
Results are shown in Table-1 and Fig-2, Fig-3, Fig-4, Fig-5 and Fig-6

**Table-1 :** Comparison between the lengths of right index (R2D) and left index (L2D) finger, right ring (R4D) and left ring (L4D) finger and right index to ring digit ratio (R2D:4D) and left index to ring digit ratio (L2D:4D) in female

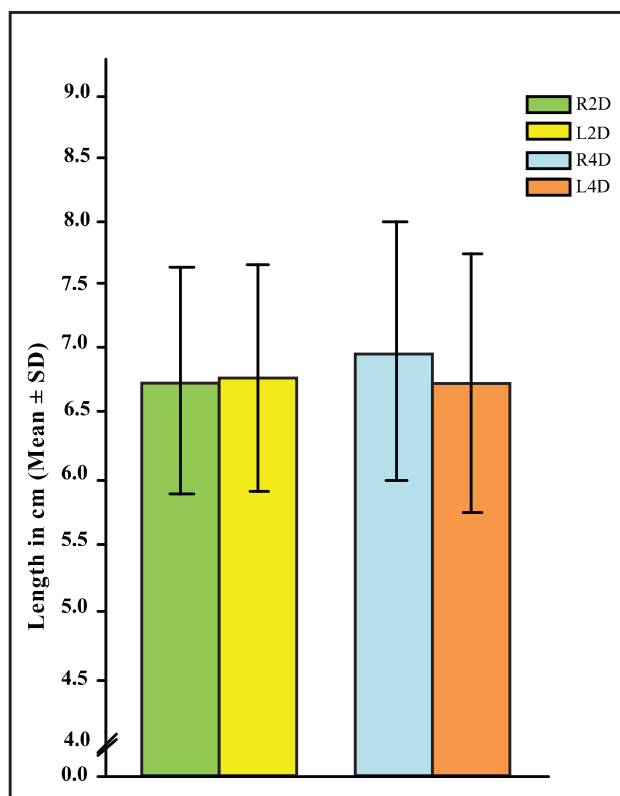
Variables	Female (n = 100)	
	mean $\pm$ SD	P-value
R2D	6.710 $\pm$ 0.369 (5.952 - 7.813)	P > 0.05 ns
L2D	6.720 $\pm$ 0.362 (5.765 - 7.912)	
R4D	6.828 $\pm$ 0.390 (6.014 - 8.074)	P < 0.001***
L4D	6.765 $\pm$ 0.388 (5.896 - 8.032)	
R2D:4D	0.982 $\pm$ 0.029 (0.931 $\pm$ 1.061)	P < 0.001***
L2D:4D	0.993 $\pm$ 0.023 (0.943 - 1.054)	

Paired Student's 't' test, ns = not significant,

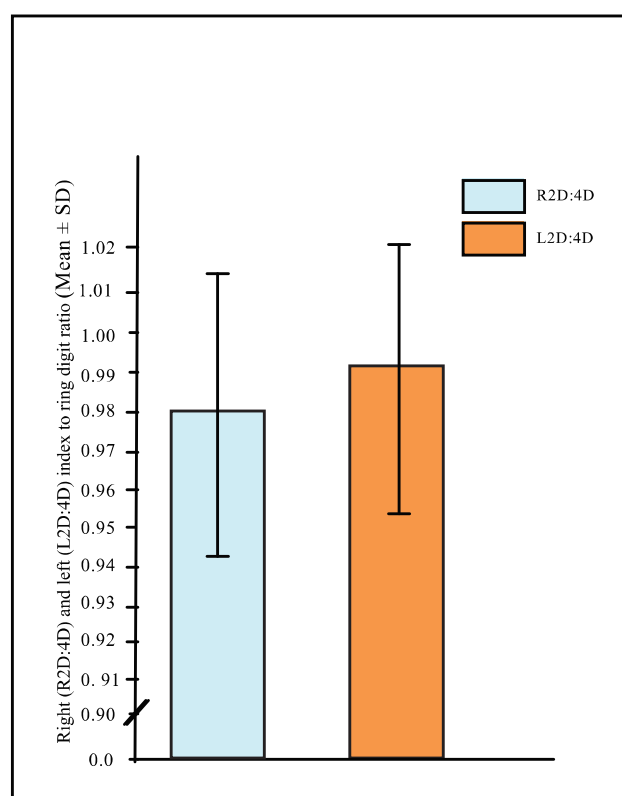
\*\*\* = significant at P < 0.0001



**Fig 1 :** Measurements of index (2D) and ring (4D) length



**Fig 2 :** Comparison between the length of right (R2D) and left (L2D) index finger and right (R4D) and left (L4D) ring finger



**Fig3 :** Right index to ring digit ratio (R2D:4D) and left index to ring digit ratio (L2D:4D) in female

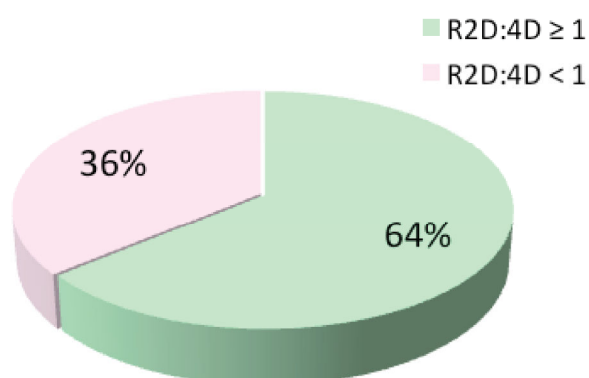


Fig.4: Right index to ring digit ratio(R2D:4D) in female

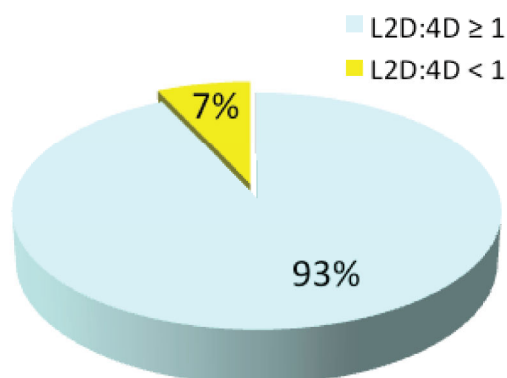
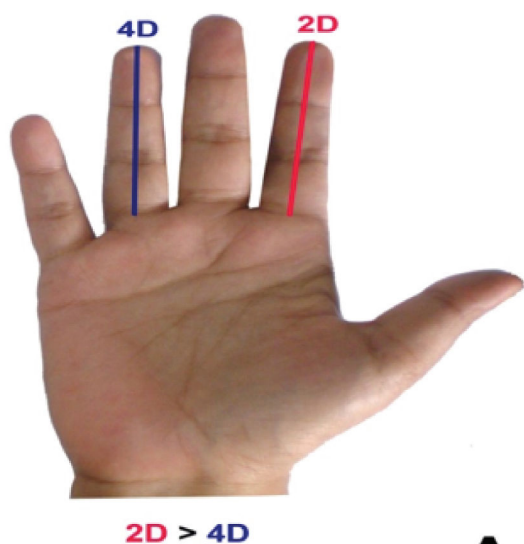
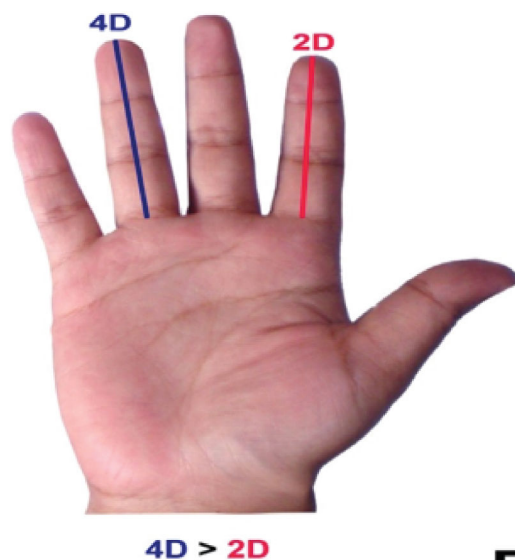


Fig.5: Left index to ring digit ratio (L2D:4D) in female



**A**



**B**

### Discussion

There was no significant differences between the length of right (R2D) and left (L2D) index finger ( $P > 0.05$  ns). Significant difference between the length of right ring finger (R4D) and left ring finger (L4D) were observed in female ( $P < 0.001$ ) where right ring finger length (R4D) was higher than left ring finger length (L4D). There was significant difference between right index to ring digit ratio (R2D:4D) and left index to ring digit ratio (L2D:4D) where left index to ring digit ratio (L2D:4D) was higher than right index to ring digit ratio (R2D:4D) in female ( $P < 0.001$ ). In this study, right index to ring digit ratio (R2D:4D) was recorded  $< 1.00$  in 36% and  $\geq 1$  in 64% subjects and left index to ring digit ratio (L2D:4D) was

recorded  $< 1.00$  in 07% and  $\geq 1$  in 93% of subjects that indicates sexual dimorphism in 2D:4D ratio is more prominent in the left hand among Bangladeshi female. The results of this study were very much familiar with the studies conducted by William et al.<sup>13</sup>, Lippa, R.A.<sup>14</sup>, Rahman Q.<sup>15</sup>, Wilson GD.<sup>16</sup>, KOSİF R. and Dirmali M. B.<sup>17</sup>, Danborn et al.<sup>18</sup> and Ibegbu A.O. et al.<sup>19</sup> McFadden D. and Shubel E.<sup>20</sup> but differ from the study of Shima M. A. et al.<sup>21</sup>

### Conclusion

Index (2D) and ring (4D) digit lengths and their ratio (2D:4D) are one of the precise method to determine sexual dimorphism. Also, study over the variations of digital lengths have great medicolegal importance to

determine age, sex and race of an individual. Doing studies on digital lengths and ratios often reveal so many mysterious characters of human hand that indicates general sexual characters and hormonal status of adult population of Bangladesh.

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## Original article

# Effect of lactation on serum high density lipoprotein & low density lipoprotein

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### Abstract

**Objective :** This study was done to observe serum high density lipoprotein & low density lipoprotein in lactating & nonlactating mother.

**Method :** The present cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, during the period of July 2010 to June 2011. A total 300 subjects were included within the age limit from 20 to 40 years of women. Among them 100 were normal healthy subjects & had child above 3 years were considered as group A (control). The rest 200 women were selected as study subject (group B) having child between the age 6 weeks to 2 years. Group B is again subdivided into group B<sub>1</sub> (100 lactating mother) & group B<sub>2</sub> (100 nonlactating mother).

**Results :** In group B<sub>1</sub> HDL was significantly higher but LDL level was non significantly higher than that of group A. In group B<sub>2</sub> serum LDL level were significantly higher than that of group A but HDL level which was significantly lower. Within the study groups serum LDL level was significantly higher in nonlactating mother than lactating mother but HDL which was significantly lower in nonlactating mother. Duration of lactation was negatively correlated with serum LDL level both in group B<sub>1</sub> & group B<sub>2</sub> but positive correlation with HDL in group B<sub>1</sub>. But the relationship was statistically significant with serum LDL in group B<sub>1</sub>. High level of HDL with higher percentage was present in lactating mother & high level of LDL with high percentage was present in nonlactating mother.

**Conclusion :** From the results of the present study it may be concluded that lactation has effect on lowering serum bad cholesterol & increase good cholesterol.

**Key words :** Lactation, serum high density lipoprotein & low density lipoprotein.

### Introduction

Breast feeding being related to both baby & mothers health status is now become a global health issue. Breast milk is the most complete form of nutrient for the good health, growth, immunity & development of the baby. Lactation that results a number of physiological adaptations exert direct effects on maternal health, some of which may confer both short and long term advantages. In the early postpartum period breast feeding promotes a more rapid return of the reproductive organs to it prepregnant

state through the action of oxytocin. It also returns the body weight & reduces the metabolic changes that occur during pregnancy<sup>1</sup>.

The American Academy of Pediatrics recommends that all infants should be exclusively breast feed through 6 months of age and that breastfeeding should continue until the infant is 1 year of age. Although 80% of US women initiate lactation, only 36 % report breast feeding and 14% report exclusive breast feeding their infants at 6 months of age<sup>2</sup>.

In a study on breast-feeding done in Bangladesh found that 60% of infants were being exclusively breast-fed and 30% predominantly breast-feed at the time of discharge from hospital. After 2 weeks at home, 75% of the mothers were breast-feeding exclusively but 25% of mothers failed to continuing exclusive breast-feeding, despite of having been counseled during their hospital stay<sup>3</sup>.

Physiological changes during pregnancy include changes in genital organs as well as change in all systems of the

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body. Physiologic adaptations during healthy pregnancy include marked insulin resistance, atherogenic dyslipidaemia, and fat accumulation. But these manifestations are largely reversed back after delivery. If these alterations are failed to reverse & persist long time after delivery then they causes long lasting adverse physiologic effects & ultimately develop metabolic syndrome<sup>4</sup>.

Lactation creates a metabolic drain & associated with favorable effect on maternal glucose homeostasis, blood lipid profile, body weight and fat distribution. Lactating women exhibits lower plasma glucose & insulin level, a less atherogenic lipid profile & greater fat mobilization during the first year of post partum than nonlactating women<sup>2,5,6</sup>. Women who do not lactate may have greater difficulty in mobilizing fat that accumulated during pregnancy resulting increased body weight & hyperlipidaemia<sup>7,8</sup>.

Findings of some studies reported that during lactation there is promote secretion of cholesterol into milk & may improve lipid profiles & reduce the risk for cardiovascular disease. So the long duration of lactation may reduce the development of atherosclerotic damage<sup>1,9</sup>.

Serum total cholesterol & serum total triglyceride concentration gradually increase during pregnancy. After delivery, serum triglyceride concentrations declines rapidly to the normal range while total cholesterol and low-density lipoprotein cholesterol declines more slowly. But TG & LDL level remain more at least 6 weeks of post partum in both lactating and nonlactating women<sup>6,10,9</sup>.

However the HDL cholesterol level remains higher after delivery in lactating mother than non lactating mother. Prolactin increases the clearance of plasma TG and subsequently increases the concentration of HDL & decrease plasma TG<sup>9</sup>.

Low level of HDL cholesterol may be the most powerful predictor of heart disease in women<sup>11</sup>.

Pregnancy related adverse changes in some metabolic risk factors like plasma LDL-Cholesterol & fasting insulin were attenuated in women who had lactated. Lactation for at least 3 months was associated with more favorable metabolic risk.

From different studies it has been observed that lactation plays a central role in mobilizing accumulated fat stores, improving lipid profile and "resetting" maternal metabolism, thereby reducing maternal risk for metabolic diseases<sup>7</sup>.

Some study found that longer breast feeding was associated with lower risk factors and less cardiovascular disease. Women who reported a life time history of more than 12 month of lactation were less likely to have hypertension, diabetics, dyslipidaemia & cardiovascular disease than women who never breast feed<sup>13</sup>.

Another large study found that women had a life time breast feeding exposure at least 2 years had lower risk for heart attack or cardiovascular disease than parous women who had never breast feed. Women who breast feed a life time of more than 2 years or longer had 23% lower risk of coronary heart disease<sup>7</sup>.

In Bangladesh, is now being a developing country women are also taking part in economy. But many of them failed to continue breast feed exclusively or adequately. As breast feeding is a birth right for every child so peoples should be aware of it. Government has taken multiple programs for improving and awareing people about breast feeding. The present study has been designed to assess the serum LDL & HDL status of lactating mother as well as in nonlactating mother.

Lactation has effect on lowering serum LDL & increasing serum HDL level. Present study will provide us knowledge about beneficial effect of breast feeding on maternal health, which will increase the public awareness of breast feeding.

## Methods

It was a cross sectional study, carried out in the Department of Physiology, Dhaka Medical College from July, 2010 to June, 2011. A total number of 300 female subjects were included within the age of 20-40 years.

Group A(control): Consists of 100 apparently healthy, non gravid & nonlactating mother having child of age above 3 years or mother not in lactation period (to compare with study group).

Group B (study group): Consists of 200 female subjects having baby between 6 weeks to 2 years or mother in lactation period but not in purperium (the period of

puerperium is avoided as most of the physiological changes during pregnancy revert back to normal with in this period) Group B is again divided into group B<sub>1</sub>: 100 lactating mother, B<sub>2</sub>: 100 non lactating mother. All subjects were selected from the pediatric indoor & out door, of DMCH and from BSMMU.

Pregnant mother with baby below 2 years or mother having adopted child or mother having baby < 6 weeks (as it is the period of puerperium) were excluded from the study. Mothers with heart disease, liver disease or kidney disease or any endocrine disease like thyroid disease were also excluded. All the subjects were requested to be empty stomach before giving blood sample. Before taking blood sample an informed written consent was taken from each subject. Ethical clearance was taken from ethical review committee of Dhaka Medical College. Data were collected in a predesigned data collection sheet. With all aseptic precaution 5 ml of venous blood was drawn from the antecubital vein. Blood was allowed to clot and then centrifuged at a rate of 3000 rpm and supernatant clear serum was separated. Serum was taken into tube and was preserved in refrigerator at - 28° c in Department of Physiology of Dhaka Medical College, Dhaka. Estimation of serum total cholesterol & triglyceride were done by biochemical end point technique in Dimension® Clinical chemistry system in same place.

Statistical analysis were done by Student's unpaired 't' test. Correlation was analyzed by Pearson's correlation test. P value < 0.05 was taken as level of significance.

## Results

In the present study mean HDL, LDL levels in lactating mothers were higher than that of baseline control group but HDL levels was statically highly significant. In non lactating mothers the mean level of HDL was lower than that of control which were statistically significant & LDL level was higher than that of control which was statistically highly significant ( $p < 0.001$ ). Within the study group the HDL level in group B<sub>1</sub> was significantly higher than the HDL level of group B<sub>2</sub> & LDL was lower than that of group B<sub>2</sub> & was statistically significant ( $p < 0.01$ ).

Duration of lactation in group B<sub>1</sub> showed positive correlation ( $r = + 0.175$ ) with HDL level & the LDL level showed negative correlation ( $r = - 0.246$ ) was statically

significant. In group B<sub>2</sub> both HDL & LDL level showed negative correlation ( $r = - 0.142, r = - 0.134$ ). Among them the relationship was significant for LDL in lactating mother whereas other relationships were not statistically significant.

HDL 50 mg/dl were present in 30.8 % subjects in group A, 43.1% subjects in group B<sub>1</sub> & 26.2% subjects in group B<sub>2</sub>. LDL > 99mg/dl were present in 15% subjects in group A, 35% subjects in group B<sub>1</sub> & 50% subjects in group B<sub>2</sub>

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**Table-I**  
**High density lipoprotein**  
**and low density lipoprotein in different groups (n=300)**

Groups n	High density lipoprotein (mg/dl) (Mean±SD)	Low density lipoprotein (mg/dl) (Mean±SD)
A 100	49.32±6.71	92.72±28.77
B1 100	54.92±10.02	97.39±23.09
B2 100	46.36±9.91	106.64±25.81

**Statistical analysis**

Groups	High density lipoprotein (p value)	Low density lipoprotein (p value)
A vs B <sub>1</sub> 0.0001***	0.207ns	0.207ns
A vs B <sub>2</sub> 0.014*	0.0001***	0.0001***
B1 vs B <sub>2</sub>	0.0001***	0.008**

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Group A : Mother not in lactation period (control group)

Group B : Mother in lactation period (study group)

Group B<sub>1</sub> : Lactating mother

Group B<sub>2</sub> : Non lactating mother

n = Number of subjects

ns = Not significant

\* = Significant at P<0.05

\* = Significant at P<0.01

\*\*\* = Significant at P<0.001

**Table II**  
**Correlation of duration of lactation with different parameters**  
**in lactating and non lactating groups(n=200)**

Parameters	Group B <sub>1</sub> (n=100)		Group B <sub>2</sub> (n=100)	
	rp	r	p	
High density lipoprotein	+0.175	0.081ns	0.142	0.159ns
Low density lipoprotein	0.246	0.014*	0.134	0.185ns

Pearson's correlation coefficient (r) test was performed to compare relationship between parameters. The test of significance was calculated and p value <0.05 was accepted as level of significance.

Group B<sub>1</sub> : Lactating mother

Group B<sub>2</sub> : Nonlactating mother

n = Number of subjects

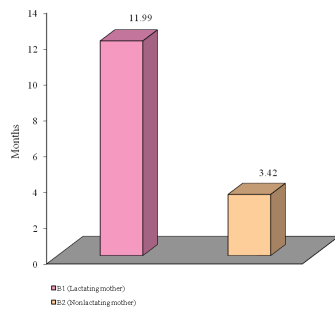
ns = Not significant

\* = Significant at P<0.05

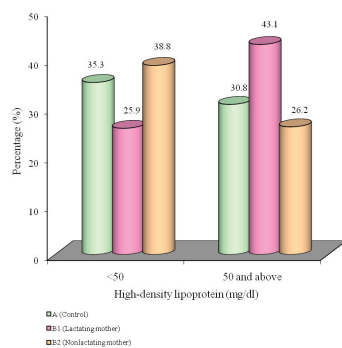
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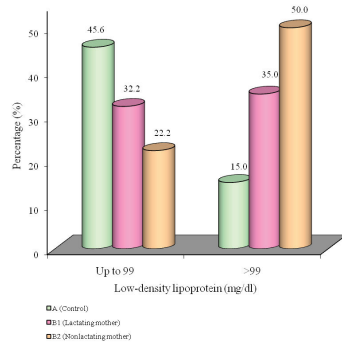
**Fig: 2**  
Mean duration of lactation in lactating and nonlactating groups



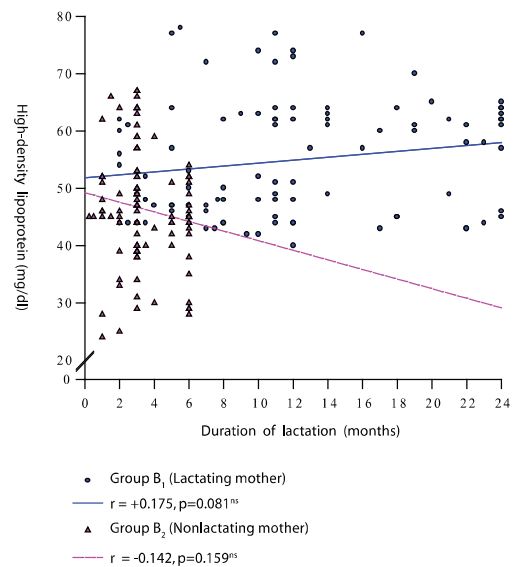
**Fig: 2.3**  
Frequency distribution of subjects by high-density lipoprotein in different groups



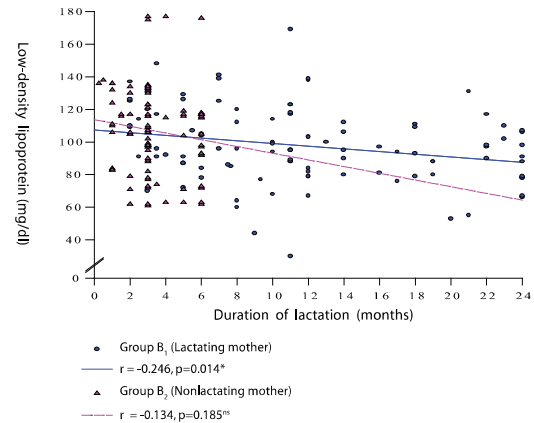
**Fig: 3**  
Frequency distribution of subjects by low-density lipoprotein in different groups



**Fig: 4**  
Correlation between duration of lactation and high-density lipoprotein in group B<sub>1</sub> and B<sub>2</sub>



**Fig: 5**  
Correlation between duration of lactation and low-density lipoprotein in group B<sub>1</sub> and B<sub>2</sub>



**Discussion:**

The present study was carried out to observe serum HDL & LDL in lactating (group B<sub>1</sub>) & nonlactating mother (group B<sub>2</sub>) and also in age matched apparently healthy adult female who are not in lactation period (group A) for comparison.

Distributions of the parameters were observed among the groups. All the parameters were also correlated with duration of lactation in both study groups to observe any relationship with the duration of lactation.

In the present study, findings of all the parameters in healthy subjects or baseline control group were almost within normal range and also similar to those reported by the other investigators from different countries<sup>14,15,7</sup>. However no published data of these study parameters of lactating mother are available for comparison in our country.

In the present study mean LDL levels in lactating mothers were nonsignificantly higher but HDL level was significantly higher than that of control subjects. In nonlactating mothers the mean LDL levels were higher but HDL level was lower than that of control subjects & was statistically significant. The present study showed significant lower level of LDL & significant higher level of HDL in lactating mother than nonlactating mother. Mean duration of lactation showed negative correlation with LDL in lactating mother & HDL & LDL in non lactating mothers. But positive correlation was observed with HDL level in lactating mothers.

Some researcher suggested that 13 weeks post weaning plasma HDL cholesterol were higher among women who lactated more than 3 months than women lactated less than 3 months. They also stated that women continue to breast feed for 1 year showed higher level of HDL persist until weaning which prevent development of hypertension & cardio vascular disease<sup>9,6,17</sup>.

Some study found that healthy lactating women have higher level of HDL cholesterol at 6 weeks postpartum in lactating mother compared to nonlactating mother<sup>6</sup>.

A research work showed that a significant decrease of LDL & increase of HDL within the post partal years. They also suggested that serum TG decrease with in 3 months after delivery in lactating mother but no more significantly later. Lactating mother showed higher HDL & cholesterol ratio than nonlactating mothers. This is also in agreement with the present study<sup>18</sup>.

Some study stated that pregnancy associated increase in

serum triglyceride & total cholesterol level resolve more rapidly in women who breast feed than women who do not. Lactating women also have higher level of HDL cholesterol than that of nonlactating mother. They reported that these favorable changes in lipid metabolism persist after weaning & has a long lasting effect on maternal metabolism. This study is also in agreement with the present study<sup>17,19</sup>.

Lactating mother secrete large amounts of cholesterol into their milk averaging 15-20 mg cholesterol / 100 ml of milk among the women who feed exclusively to the baby. As a result there is an output of average 150 mg/ day which roughly equals the amount of cholesterol lost by cholesterol lowering drug. Lactation decreases the cholesterol level which prevents the risk of cardiovascular disease<sup>9</sup>.

Milk triglycerides & cholesterol are known to be derived from lipoproteins as well as denovo synthesis in the mammary gland. Prolactin activates an enzyme in the mammary gland that increases the clearance of plasma TG and increases the concentration of HD<sup>6,9</sup>.

Substantial demand for TG in healthy lactating mother to enhance VLDL catabolism & generation of increased HDL components via transfer of surface remnants<sup>6</sup>.

**Conclusion**

Present study revealed that lactating mother has lower LDL & higher HDL level than that of non lactating mother. Higher percent of frequency distribution of HDL & lower percent of frequency distribution of LDL level was seen in lactating mother than that of non lactating mother. Duration of lactation has significant negative correlation with LDL level in lactating mother.

From the above discussion it may be concluded that lactation has effect on lowering serum LDL & increasing serum HDL level.

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## Original Article

# Assessment of insulin resistance in adult obese female of Dhaka City.

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### Abstract

**Objective :** To assess the insulin resistance in adult obese female of Dhaka City. As insulin resistance represents the underlying mechanism of type 2 diabetes, hypertension and cardiovascular diseases, this parameter would be an important clinical and biochemical determinant.

**Methods :** This cross sectional analytical study was conducted in the Department of Physiology, Dhaka Medical College from July 2012 to June 2013. Fifty obese females ages ranging from 20-40 yrs were included in the study group (Group B) and were selected from obesity clinic of BIRDEM, Dhaka and from different areas of Dhaka city. Again, fifty ages matched, healthy female subject selected as control (Group A) and also selected by personal contact from different areas of Dhaka city. Fasting serum insulin level was measured by ELISA. Serum glucose level was measured by glucose oxidase method. For statistical analysis, unpaired Student's test and Pearson's correlation coefficient (r) test were performed as applicable using SPSS Version-20.

**Result :** HOMA-IR was significantly ( $P<0.001$ ) higher in the study group than that of control.

**Conclusion :** This study concludes that there is a positive relationship between obesity and insulin resistance. Therefore, in obese, screening for insulin resistance may be helpful to counteract the adverse effects of hyperinsulinemia.

**Key word :** Obesity, insulin resistance, HOMA-IR (homeostasis model assessment of insulin resistance)

### Introduction

Obesity is considered to be a major nutritional disorder in the United States and in many parts of the industrialized world. The pathophysiology of the obese and their tendency for chronic disease has been of growing interest over the past few years<sup>1</sup>.

Obesity is defined medically as a state of increased body weight specifically adipose tissue in a magnitude to produce adverse health consequences<sup>2</sup>. The most widely used method to assess obesity is the body mass index (BMI). On the basis of the respective health-related risk

factors, in Asian populations BMI  $\geq 25.0$  kg/m<sup>2</sup> is called obese<sup>3,4</sup>. Obesity is present in 35.8% of adults living in the U.S.<sup>5</sup> and 1.4% in Bangladesh<sup>6</sup>. Obesity increases the risk of diabetes, hypertension, cardiovascular diseases, certain cancers, liver and gall bladder diseases, osteoarthritis, respiratory diseases and stroke<sup>7</sup>. Various metabolic changes occurs in obesity such as increased hepatic very low density lipoprotein (VLDL) output, increased adipose tissue lipogenesis and VLDL uptake. And these abnormalities are secondary to insulin resistance<sup>8</sup>. Anthropometric indices, central body fat distribution and insulin resistance predict these metabolic changes in adult obese subject<sup>9</sup>.

Insulin resistance is defined as a condition in which insulin's target organs are resistant to its action, so that higher concentrations of this hormone are needed to achieve a normal biological effect<sup>10</sup>. The "gold standard" technique to evaluate insulin resistance is the euglycemic hyperinsulinemic clamp. But the homeostasis model assessment of insulin resistance index [ $\text{HOMA-IR} = \text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glycemia (mmol/L)} / 22.5$ ] now-a-days can be considered the best non invasive surrogate marker of insulin resistance<sup>11</sup>. HOMA-IR  $>2$  was considered as insulin-resistant in obese subjects<sup>12,13</sup>. Pathological changes associated with insulin resistance and compensatory hyperinsulinemia are altered glucose

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metabolism, endothelial dysfunction, hypercoagulability, haemo dynamic changes, chronic inflammation, hypertension, decreased high-density lipoprotein cholesterol concentration, increased triglyceride concentration and non-insulin-dependent diabetes mellitus<sup>14</sup>. South Asians are at higher risk than Caucasians for the development of obesity and obesity-related non-communicable<sup>3</sup>. Urban population of Bangladesh showed higher prevalence [about 76.5%] of insulin resistance<sup>15</sup> than that was found in Asians [14% men and 19% women]<sup>16</sup>.

Insulin resistance is common in obese individuals. Jones et al<sup>17</sup>. observed in age matched obese and non-obese women and stated that plasma glucose, insulin and C-peptide concentrations were significantly higher in obese women in response to intravenous glucose infusion.

Again, a positive correlation was found by Kopelman<sup>18</sup> between central obesity and insulin resistance. An increased insulin response in obese during oral glucose load was found.

Furthermore, Chen et al<sup>19</sup>. conducted a study over the participants of third National Health and Nutrition Examination Survey. From their study, they showed that persons with high insulin resistance had significantly higher BMI and waist circumference.

From the above studies it has been observed that in obese individual, high fasting serum insulin level and insulin resistance act as risk factors for various diseases. This study may help to create awareness among the physicians and the obese female of Bangladesh regarding the damaging effect of insulin resistance.

### Materials & Methods

This is a cross sectional analytic study was conducted in Department of Physiology, Dhaka Medical College Dhaka from July 2012 to June 2013. A total number of 100 female subjects with the age ranging from 20-40 yrs were included in this study. Among them 50 obese females with BMI 25-39.9 Kg/m<sup>2</sup> were included in study group and age and sex matched 50 healthy subjects were considered for comparison. They were selected from obesity clinic of BIRDEM, Dhaka and also by personal contact from different areas of Dhaka city. All the subjects were excluded from Diabetes mellitus, hypertension or any other endocrine diseases. Anthropometric measurement was done. After overnight fasting, 5 ml of venous blood was collected at 8 am from every subject for estimation of serum glucose, serum insulin level. Insulin was measured by ELISA method. Assessment of insulin

resistance was done by calculation of HOMA-IR.

Data were analyzed by unpaired Student's 'T' test and Pearson's correlation coefficient (r) test.

### Results

All the parameters were expressed as mean  $\pm$  SD. The comparison of the values was done among two groups. Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.

Group A :Control (Adult healthy female)

Group B : Study group (Adult obese female)

n = Number of subjects

BMI and WHR of two groups are shown in Table I and they are significantly higher in obese female than healthy female. Insulin resistance (HOMA-IR) in both groups is presented in table-II and highly significant mean HOMA-IR is found in obese female than healthy female.

Again, figure-1 showed that among the study subjects, HOMA IR <2 in 0% and HOMA IR > 2 100.0% subjects.

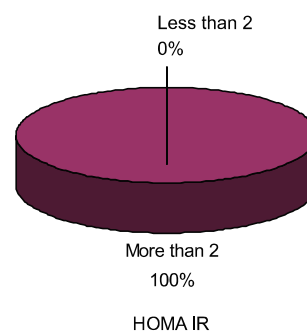
Figure 2 and 3 showed HOMA-IR was positively correlated with BMI (p<0.05) WHR (p<0.05).

**Table I :** BMI and Waist Hip ratio (WHR) in both groups(n=50)

Parameters	Group A (n=50)	Group B (n=50)	P value
BMI	22.18 $\pm$ 2.00	30.85 $\pm$ 3.65	<0.001
WHR	0.78 $\pm$ 0.03	0.86 $\pm$ 0.05	<0.001

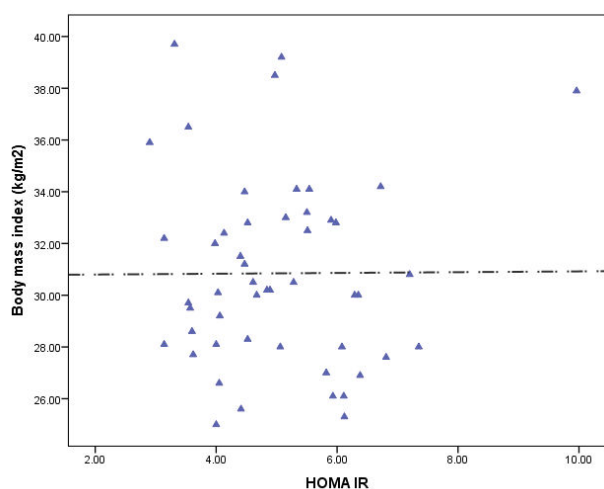
**Table II :** HOMA-IR in both groups (n=50)

Parameters	Group A (n=50)	Group B (n=50)	P value
HOMA-IR	2.19 $\pm$ 0.60	5.02 $\pm$ 1.34	<0.001

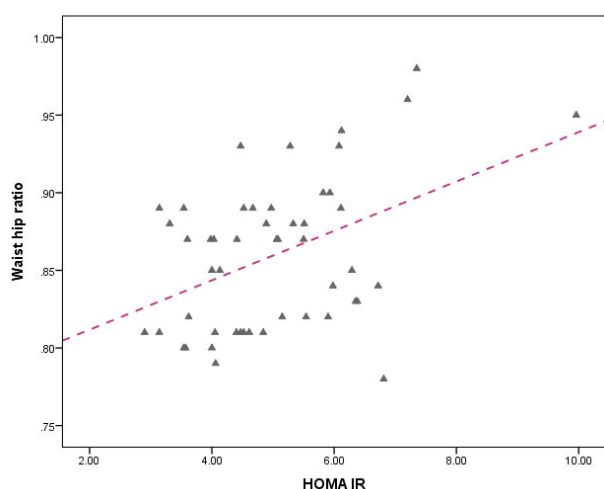


**Figure 1:** Distribution of the subjects by HOMA-IR in Study group (n=50)





**Figure 2 :** Correlation between BMI and HOMA- IR in adult obese female (n=50)



**Figure 3 :** Correlation between WHR and HOMA- IR in adult obese female (n=50)

### Discussion

In this study mean HOMA-IR was significantly higher in obese female than healthy female. Moreover, 100% of the study subject were found insulin resistance (HOMA-IR>2). Again, HOMA-IR showed positive correlation with BMI and WHR which favors this findings. So, in this study insulin resistance have been found in obese female. The postulated mechanism for development of insulin resistance in obese female may be due to high level of plasma free fatty acids. The increased level of fatty acid stimulates the intra-mitochondrial acetyl CoA/CoA ratio and NADH/NAD<sup>+</sup> ratio which inactivate pyruvate

dehydrogenase. Due to inactivation of pyruvate dehydrogenase, intracellular citrate concentrations increases which again inhibits phosphofructokinase. So, phosphofructokinase cannot phosphorylate glucose-6-phosphate. Subsequently, accumulation of glucose-6-phosphate occurs which inhibits hexokinase II activity. So, glucose cannot be converted in to glucose-6-phosphate. As a result, intracellular glucose concentration rises and decreases in glucose uptake by the cell. Thus fatty acid interferes in insulin stimulation of GLUT 4 activity. Thereby insulin resistance develops<sup>20</sup>. Again, increasing intracellular fatty acid metabolites, such as diacylglycerol, kinase cascade, leading to phosphorylation of serine/threonine sites on insulin receptor substrates. Serine-phosphorylate forms of these proteins fail to associate with or to activate PI 3-kinase, resulting in decreased activation of glucose transport and other downstream events<sup>21</sup>.

### Conclusion

This study revealed that, obese female may develop insulin resistance. Screening for insulin resistance may be helpful to counteract the deleterious effects of insulin resistance. So, assessment of insulin resistance in obesity will minimize the obesity related other complications.

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## Original article

# Assessment of serum creatinine and lipid profile in type 2 diabetes mellitus patients

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### Abstract

**Objectives :** To assess the serum creatinine, lipid profile and blood pressure in type 2 DM patients.

**Methodology :** This was a cross sectional comparative study. Data were collected from 400 type 2 DM patients (200 males and 200 females) attending to BIRDEM OPD. Variables measured included-serum creatinine, blood sugar (FBS, ABF), lipid profile (TG, TC, LDLC, and HDLC) and blood pressure.

**Results :** Statistical analysis were performed by applying student T test and Pearson's correlation co-efficient at .0001 and 0.05 level of significance respectively. Blood sugar was higher than normal in both male and female (FBS=8.79±.20, 8.64±0.22 respectively and ABF=12.15±0.27, 11.8±0.29 respectively). Though the value of FBS and ABF was higher in male than in female, significant difference between the groups was found only in ABF (p=.000). TG level was also higher in two groups of study subjects with male level is slightly more than female (194.99±6.72 and 185.21±15.51 respectively) with no significant difference between the groups (P>.05). Total cholesterol and LDLC level was within normal physiological level in both groups, whereas the level was higher in female in comparison to male (TC=166.16±3.04 & 184.44±3.33 respectively, LDLC=88.66±2.59 & 109.68±2.59 respectively), showing significant difference between the groups (P=.000). There was significant elevation of creatinine level above normal in male (1.677±0.018), however the level was within normal in female (0.924±0.018). Both systolic and diastolic blood pressure was within normal level in both male and female, showing no significant difference between the groups.

**Conclusion :** Dyslipidaemia, gender, age and serum creatinine are associated with type 2 DM. While age and gender are non modifiable risk factors. Steps should be taken to monitor and control the serum creatinine and lipid profile values of male and female diabetes.

**Key words :** Dyslipidaemia, Nephropathy, Type-2 Diabetes Mellitus.

### Introduction

Dyslipidaemia is identified as a risk factor in the development of type 2 Diabetes mellitus (DM) complications and it contributes significantly to the development of macrovascular complications<sup>1</sup>. Patients with type 2 DM often present with adverse lipoproteins disorders<sup>2</sup>. The patterns of dyslipidaemia in non-African type 2 Diabetes mellitus populations have been evaluated and the prognostic significance of lipoprotein fractions for the future risk of macrovascular complications defined<sup>3</sup>.

Jarikre et al, examined total cholesterol: high density lipoprotein cholesterol (HDL) ratios in Nigerians and

defined a new emerging pattern of transitional dyslipidaemia in Nigerians<sup>4</sup>. However, their study was among non-diabetic Nigeria population. The reported prevalence of diabetic dyslipidaemia varies from 25%-60%<sup>5</sup>.

In this study, the serum lipid abnormalities in patients with type 2 DM, was examined with the aim of elucidating the type of lipoprotein disorders associated with diabetic nephropathy and diabetic hypertension in type-2 diabetics. It is hoped that the outcome of this study will draw specific attention to the management of dyslipidaemia in patients with complicated type 2 DM especially patients with diabetic nephropathy and diabetic hypertensive.

### Methods

**Selection of Patient :** The study populations were diabetic patients attending the OPD of BIRDEM. A total of 400 type 2 DM patients and out of which (200 were male and 200 were female diabetics) were studied. The patients were randomly selected and were aged between 30-80 years. Diabetes mellitus was diagnosed according to WHO criteria<sup>4</sup> and classified as type 2 also using WHO criteria<sup>4</sup>. Hypertension was diagnosed and defined as blood pressure 140/90mmHg<sup>3</sup>. Subjects with serum creatinine

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< 124mmol/L (< 1.4mg/dl) and > 124mmol/L (> 1.4mg/dl) were assumed to have normal and impaired renal function respectively. The individual blood pressure was measured by sphygmomanometer at sitting position. Optimal systolic blood pressure is <120mm of Hg, normal SBP is <130 mm of Hg and high normal SBP is 130-139mm of Hg<sup>6</sup>. Optimal diastolic blood pressure is <80mm of Hg, normal DBP is 85 mm of Hg and high normal DBP is 85-89 mm of Hg<sup>6</sup>. All subjects gave informed consent after due explanation by the researcher. Ethical clearance was sought and obtained for the study.

### Laboratory assay methods

The subjects were fasted overnight (12-14 hrs) and 10mls of venous blood was obtained from the ante-cubital veins after routine aseptic procedure. The lipids were assayed using already standardized and well-established methodologies<sup>7-9</sup>. All assays were performed using kits manufactured by Human Diagnostic Laboratory (Germany). Total cholesterol assay was done using the modified Liebermann-Burchard's method of Abell et al,<sup>10</sup>. HDL-cholesterol by precipitation method<sup>11</sup>. Triglyceride was assayed using enzymatic colorimetric method after hydrolysis of the triglycerides<sup>12</sup>. LDL cholesterol was calculated by indirect method, using Friedewald et al equation<sup>9</sup>; summarized as follows:

LDL-cholesterol = Total Cholesterol- (HDL-cholesterol + TG/5)<sup>9</sup>.

Serum creatinine was measured by Jaffe reaction method in semiautoanalyzer<sup>8</sup>.

### Statistical analysis

Statistical analysis was performed. Means and standard deviations were determined for quantitative data, and frequency determined for categorical variables. Student-t test was used to test for significant association. Analysis of variance was used to compare multiple means, while Chi-squared test was used to analyze group differences for categorical variable. P Value<0.05 was considered statistically significant.

## Results

**Table-I :** Distribution of study subjects by age and sex.

Age	Distribution		Male		Female	
	N	%	N	%	N	%
30-40	86	21.7	34	17.8	52	25.7
41-50	126	31.8	54	27.4	72	35
51-60	116	29.3	64	30.5	52	27.7
61-70	62	14.6	38	19.8	24	9.4
71-80	10	2.5	10	51.1	0	0
Total	400	100	200	50	200	50

**Table-II :** Various biochemical parameters of DM in male and female.

Parameters	Male (Mean±SEM)	Female (Mean±SEM)	P value
FBS	8.79±0.20	8.64±0.22	0.607
ABF	12.15±0.27	11.81±0.29	0.000
TG	194.99±6.72	185.21±5.51	0.261
TC	166.16±3.04	184.44±3.33	0.000
LDLC	88.66±2.59	109.68±2.59	0.000
HDL	38.28±0.48	39.02±2.59	0.330
Creatinine	1.677±0.018	0.924±0.018	0.000
Systolic blood pressure	122.02±13.94	121.439±14.53	.977
Diastolic blood pressure	78.88± 10.07	79.35±7.61	.784

Table-I shows the distribution of study subjects by age and sex. Total study subjects were 400, out of which 200 male(50%) and 200 female(50%). 30-40 years aged study subjects were 86 in total, out of which male-34 and female-52. 41-50 years total study subjects were 126, out of which male 52 and female-72. Study subjects between the age of 51-60 were 116, out of which male-64 and female-52. 61-70 years study subjects were 62, where male includes 38 and female-24. Total number of study subjects between the age of 71-80 years was 10, which includes only male (no female in this age group).

Table ii shows, Blood sugar was higher than normal in both male and female (FBS=8.79±.20, 8.64±0.22 respectively and ABF=12.15±0.27, 11.8±0.29 respectively). Though the value of FBS and ABF was higher in male than in female, significant difference between the groups was found only in ABF (p=.000). TG level was also higher in two groups of study subjects with male level is slightly more than female (194.99±6.72 and 185.21±15.51 respectively) with no significant difference between the groups (P>.05). Total cholesterol and LDLC level was within normal physiological level in both groups, whereas the level was higher in female in comparison to male (TC=166.16±3.04 & 184.44±3.33 respectively, LDLC=88.66±2.59 & 109.68±2.59 respectively), showing significant difference between the groups (P=.000). There was significant elevation of creatinine level above normal in male (1.677±0.018), however the level was within normal in female (0.924±0.018). Both systolic and diastolic blood pressure was within normal level in both male and female, showing no significant difference between the groups.

## Discussion

Abnormal lipid profile, gender, age and serum creatinine are associated with type 2 diabetes. The cause of the lipid alteration among type 2 DM subjects is differential insulin distribution<sup>13</sup>, which leads to increase in VLDL and triglyceride production through hepatic hyperinsulinaemia; this is combined with decreased catabolism of triglyceride-rich lipoprotein due to relative peripheral insulin deficiency<sup>14</sup>. Clinical and experimental studies have highlighted the potential role of dyslipidemia in the development of microalbuminuria and diabetic nephropathy. Mesangial, tubulo-interstitial, and glomerular changes in the kidney have been associated with lipid levels. In animal models of diabetes, treatment of hyperlipidemia with statins has been associated with reduced glomerular injury<sup>15</sup>.

Raised TG have also emerged as a predictor for the development and progression of renal complications<sup>16</sup>. Based on these data, it appears that measurement of plasma lipids can add to the prognostic value of albumin excretion in the prediction of subjects at risk of diabetic nephropathy<sup>16</sup>.

In our study we found that both blood sugar, TG level was higher than normal in both male and female but male level more than that of female. Total cholesterol and LDL-C level was normal in both sex groups. The level of HDL-C was slightly lower than normal in two groups whereas serum creatinine level was elevated beyond normal limit only in male but not in female. Again blood pressure of both the study groups were normal. Our study corresponds with the study of Idogun ES et al who found dyslipidemia in normotensive diabetics patients, higher in patients with diabetic hypertension and very gross in patients with diabetic nephropathy<sup>17</sup>. Low-density lipoprotein cholesterol levels was reported to be normal in DM by Ruderman et al.<sup>18</sup> Our study is also consistent with that study.

Moreover we got higher TG level in type-2 male diabetics developing nephropathy. Bonnet F et al. found Potential influence of lipids especially TG in diabetic nephropathy<sup>19</sup>. Our study is consistent with that study.

## Conclusions

Dyslipidaemia, gender, age and serum creatinine are associated with type 2 DM. While age and gender are non modifiable risk factors. Steps should be taken to monitor and control the serum creatinine and lipid profile values of male and female diabetes.

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# **Review Articles**

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## Review article

# Effect of Zinc and Copper on RTI in children

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### Abstract

Zinc and copper are trace element, essential for human health and their deficiency were found to cause various infections. Respiratory tract infection in children is one of the main cause of morbidity in children of developing countries like Bangladesh. To make update knowledge on the role of these trace elements on RTI, we made this review. We conducted a systematic literature search of published articles related to zinc, copper, malnutrition and respiratory tract infection. The literature survey found that deficiency of zinc and copper have profound effects on RTI in children.

Key words : Zinc, copper, RTI.

### Introduction

Respiratory tract infection is one of the important cause of death in children under 5 years of age in developing countries<sup>1,2</sup>. A high proportion of this death is due to acute lower respiratory tract infections<sup>3,4</sup>. Zinc and copper are now considered as essential micronutrients for our body<sup>5</sup>. During recent years, much interest has been shown to the serum levels of important micronutrients like zinc and copper in the children. Some investigators reported that lower level of zinc and copper increase the susceptibility to recurrent infections in children<sup>6</sup>. Some studies have shown that changes in serum and urinary levels of zinc and copper in children suffering from respiratory tract infection<sup>7-9</sup>. Only a few data were available on micronutrient status in children with respiratory tract infection in our country<sup>10-13</sup>.

Trace elements (micronutrients) are those elements present in parts per billion concentrations in biological fluids or tissues<sup>14</sup>. Zinc is essential micronutrient for human, animals and plants<sup>15</sup>.

### Physiologic consideration of trace elements

Normal reference value of serum zinc is 70-150 µg/dl<sup>16</sup>.

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Normal reference value of serum copper is, in children 80-190 µg/dl, in adult male 70-140 µg/dl, and in female is 80-155 µg/dl,<sup>16</sup>

Estimation of serum zinc and copper were done by atomic absorption spectrophotometry<sup>17</sup>.

### Zinc and RTI

Serum zinc level may be affected by infections<sup>18,19</sup>. Different investigators observed lower level of zinc in children suffering from respiratory tract infection<sup>8,9,12,20,21</sup>.

However, some investigator observed lower serum zinc level in children suffering from recurrent respiratory tract infection<sup>8,9,12,21</sup>.

Zinc supplementation is the criteria for diagnosis of zinc deficiency<sup>22</sup>. It was observed that zinc supplementation reduced the duration of common cold in children<sup>23</sup>.

On the other hand, some observers observed a reduced attack of respiratory tract infection in children after zinc supplement<sup>23-27</sup>.

On the contrary, some observed that there is no improvement after supplementation of RTI in children<sup>28-30</sup>.

Urinary zinc level is higher in children who have lower serum zinc level<sup>8,31</sup>. Higher urinary zinc level was also observed in children with RTI<sup>8</sup>. Again, it was observed decreased levels of urinary zinc associated with decreased serum zinc<sup>16</sup>.

In any type of acute infection, hypozincemia may occur due to shifting of zinc from serum to storage tissues, mainly liver<sup>32</sup>. Again, increased utilization may also act as a contributory factor for this lower serum zinc level in patients suffering from various inflammatory diseases<sup>33</sup>. Some observer also suggested that hypozincemia may be due to low dietary intake<sup>34,35</sup>, which usually occurs in

children of RTI. On the other hand, some suggested that lower serum zinc level might also occur due to its higher urinary excretion<sup>36</sup>.

### Copper and RTI

Copper deficiency increases the incidence of RTI<sup>37</sup>. On the contrary, no change of serum copper level in recurrent respiratory tract infection in comparison to that of healthy children<sup>13,21</sup>. On the other hand, a higher serum copper level in recurrent respiratory tract infection was observed<sup>6</sup>. Higher urinary copper level is associated with lower level of serum copper<sup>38</sup>.

Some investigators suggested that, serum copper and zinc usually maintain an inverse relationship<sup>39,40</sup>. Usually copper deficiency is rare in clinical practice<sup>41</sup>.

Children suffering from protein-energy malnutrition has zinc and copper deficiency<sup>42,43</sup>. It has been seen that the increased incidence, severity and mortality of respiratory tract infection are strongly associated with malnutrition<sup>44,45</sup>.

The attacks of acute respiratory tract infection were more frequent among immune-deficient children<sup>46-48</sup>. On the other hand, zinc supplement improves immune response of the body<sup>27,28</sup>.

### Conclusion

Finding from different studies, effect of zinc and copper on respiratory tract infection is not consistent, but it should be noted even though that several studies have shown a positive effect of these micronutrient on respiratory tract infection. Thus, if well targeted, supplement of these micronutrients could be a powerful intervention to reduce the morbidity from RTI among children from developing countries, like Bangladesh.

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## Case Report

# Radiological diagnosis of right atrial isomerism with cardio-vascular anomalies

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### Abstract

Right atrial isomerism or asplenia with cardiovascular anomalies, also known as ivemark syndrome is an example of a heterotaxy syndrome. These uncommon congenital disorders are characterized by defects in the heart, spleen and paired organs such as the lungs and kidneys. A 7 years old boy referred to radiology & imaging department of National Heart Foundation Hospital & Research Institute for CT pulmonary angiogram for congenital heart disease from NICVD Dhaka. The patient had exertional dyspnoea, repeated common cold, retarded growth & loss of appetite from last 05 years. X-ray chest findings were fullness of pulmonary conus, apex of the heart on the left side & fundal gas on the right side. Echo-cardiogram showed large single ventricle with single AV valve with double outlet, severe infundibular & valvular pulmonary stenosis (PPG-95 mm Hg) with mild to moderate AV valve regurgitation with good ventricular systolic function. CT pulmonary angiogram was done. The important findings obtained were right atrial isomerism, Bronchial isomerism, evidence of translocation of the inferior vena cava to the left of the abdominal aorta, both of which were on the left of the spine, single ventricle, stenosed pulmonary infundibulum & bi-cuspid pulmonary valve. There were also secundum as well as primum types of atrial septal defect, anomalous single origin of coronary artery from the non-coronary sinus of valsalva, asplenia, mid line liver and mal-rotated gut.

Key word : Right atrial isomerism, asplenia, heterotaxy syndrome

### Introduction

Asplenia with cardiovascular anomalies, also known as Ivemark syndrome and right atrial isomerism.<sup>[1]</sup> Right atrial isomerism is named for its discoverer, Swedish pathologist Biörn Ivemark<sup>[2]</sup>. Another name is "asplenia-cardiovascular defect-heterotaxy"<sup>[3]</sup> is an example of a heterotaxy syndrome.

Heterotaxy syndrome or situs ambiguous is a disturbance in the usual left and right distribution of the thoracic and abdominal organs which does not entirely correspond to the complete or partial mirror image. It occurs from an early embryological developmental disturbance with most cases being sporadic. It is also classified under the group of cardiosplenic syndromes.

### Types of heterotaxy syndrome

There are different forms of heterotaxy syndrome. All usually involve heart defects, of varying type and severity.

### Asplenia or right atrial isomerism

In right atrial isomerism, both atria of the heart are morphological right atria leading to associated abnormalities in the pulmonary venous system.

In addition, individuals with right atrial isomerism develop asplenia, a midline liver, mal-rotation of the small intestine and the presence of two morphologic right lungs. The majority of cases present at the time of birth or within a few days or weeks. Presenting signs and symptoms of the congenital heart defect may include cyanosis, breathlessness, lethargy and poor feeding.

### Polysplenia or left atrial isomerism

Individuals with left atrial isomerism, by comparison, have two morphologic left atria, polysplenia, intestinal malrotation and two morphologic left lungs<sup>[4]</sup>.

### Causes

The cause of heterotaxy is unknown<sup>[5]</sup>.

### Presentation

Its presentation dependent on severity of the isomerism and presence of associated abnormalities. Where there is congenital heart disease, presentation may be secondary to heart failure or cyanosis. Additionally, malrotation may be a presenting feature.

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### Epidemiology

The true incidence is not known, but some sources have estimated it to be around 1 per 8,000 - 25,000 live births. Approximately 20-25% is associated with the immotile cilia syndrome.

### Pathology

Bronchial anatomy accurately reflects atrial situs. The bronchial anatomy on the left and right can be recognised on a well penetrated radiograph and consists of two main bronchi that are anatomically different:

- hyperarterial bronchus (below artery) - supplies the bi-lobed left lung
- eparterial bronchus (alongside the artery) - supplies the tri-lobed right lung

In situs ambiguous, there is duplication of either the hyperarterial or eparterial bronchus. The associated atria are also duplicated and there are specific changes below the diaphragm (although not left / right-sided duplication)<sup>1</sup>.

All children with heterotaxy syndrome will require life-long care by a cardiologist.

### Case report

In this case report right atrial isomerism, congenital defects in the heart & other findings obtained has discussed elaborately.

A 7 years old boy referred to radiology & imaging department of National Heart Foundation Hospital & Research Institute for CT pulmonary angiogram for congenital heart disease from NICVD Dhaka. The patient had exertional dyspnoea, repeated common cold, retarded growth & loss of appetite from last 5 years.



### Investigations done



**X-ray chest P/A view** showed fullness of pulmonary conus, apex of the heart on the left side & fundal gas on the right side. Echo-cardiogram showed large single ventricle with single AV valve with double outlet, severe infundibular & valvular pulmonary stenosis (PPG-95 mm Hg) with mild to moderate AV valve regurgitation with good ventricular systolic function. CT pulmonary artery showed right atrial isomerism with evidence of congenital heart diseases (CHD).

### Findings of multi-slice CT Scan

Followings important findings were obtained-

**A) Right atrial isomerism:** the atrial situs is identified.



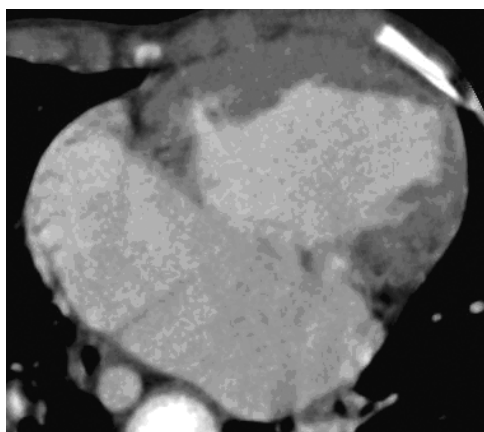
**B) Bronchial Isomerism :** both the main bronchi are symmetrically short & the upper lobe bronchi are bilaterally epi-arterial.



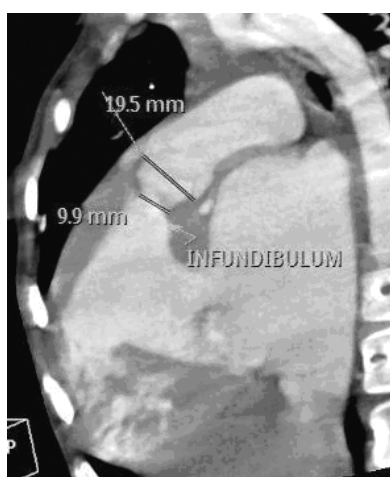
**C) Other findings of right isomerism :**



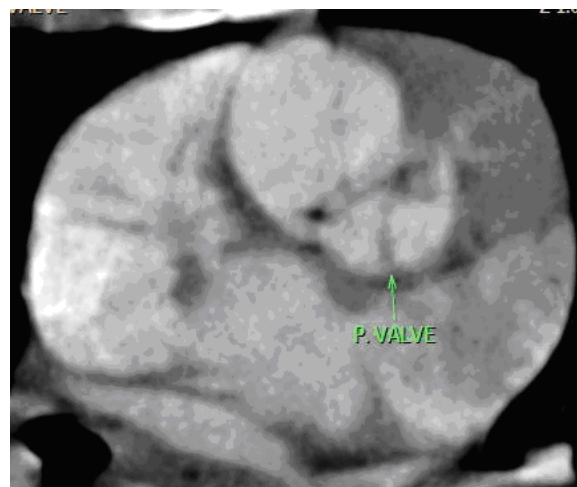
I) Evidence of translocation of inferior vena cava to the left of the abdominal aorta, both of which were on the left of the spine.



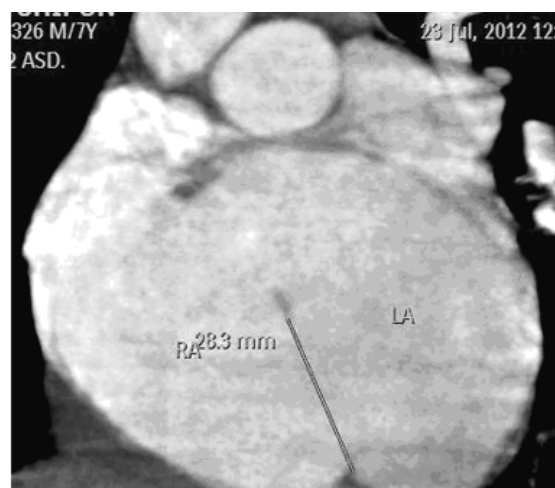
II) Single ventricle- which may be due to endo-cardial cushion defects



(III) Stenosed pulmonary infundibulum & valve



(IV) Bi-cuspid pulmonary valve.



(V) there were also secundum as well as primum types of atrial septal defect - may be due to endo-cardial cushion defects



(VI) Anomalous single origin of coronary artery from the non-coronary sinus of aorta.



(VII) Asplenia - spleen could not be delineated by USG



(VIII) liver is present in the mid line



(IX) Mal-rotated gut-stomach is present at the right hypo-chondriac region

### Discussion :

Echo-cardiography & catheter cardio-angiography are the primary cardiac imaging modalities, but both have weaknesses.

Echocardiography is limited by

- (a) A small field of view,
- (b) An acoustic window
- (c) Operator dependence.

Catheter cardio-angiography is limited by the

- (a) Overlapping of adjacent vascular structures,
- (b) Difficulty in demonstrating systemic & pulmonary vascular systems simultaneously,
- (c) Catheter-related complications (especially in young children) &
- (d) Relatively high doses of ionizing radiation & iodinated contrast material.

Computed tomography (CT) & magnetic resonance (MR) imaging have important roles in overcoming these limitations

Recently multi-slice CT plays an important supplementary role in the evaluation of patients with congenital heart disease (CHD). This modality can be used to obtain isotropic volume data & high-quality two- & three-dimensional multi-planner reformatted images can be created to accurately & systematically delineate the normal & pathologic morphologic features of the cardio-vascular system.

CT may be technically challenging & demanding in un-cooperation young children. However it can be used to systematically evaluate the aorta, Pulmonary Artery, Pulmonary Vein, Cardiac Chambers & Ventriculo-arterial connection, relationship between the upper lobe bronchi & pulmonary arteries, coronary artery, valves, systemic vein (superior/inferior venae cavae & hepatic veins) & visceral situs with a step-by-step approach.

### Conclusion

Multi-slice Multi-detector CT have distinct diagnostic value in revealing thoraco-abdominal organs & major vessels (various viscero-vascular abnormalities) which can be crucial in the diagnosis & surgical management of patients with Right Atrial Isomerism.

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