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Original Research Paper

General Surgery

HEMO-LITH: CORRELATION BETWEEN IRON DEFICIENCY ANEMIA AND CHOLELITHIASIS USING COMPLETE BLOOD COUNTS AS THE SOLE GUIDE-A CASE CONTROL STUDY

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ABSTRACT Iron deficiency anemia has been implicated as one of the factors in the pathogenesis of cholelithiasis. Micronutrients such as iron, zinc, copper, etc have been shown to be associated with cholelithiasis. Iron is a co-factor for the enzyme nitric oxide synthase (nos) which is responsible for the production of nitric oxide. Reduced levels of nitric oxide are associated with dysmotility of gall bladder wall. Also, iron deficiency has been seen to be associated with bile super saturation in gallbladder. We have reconfirmed this association with case control study model, using only complete blood count parameters to define iron deficiency anemia. This has avoided extra financial burden on the patients which is of utmost importance in the region with compromised socio-economic statistics.

KEYWORDS : Cholelithiasis, Iron Deficiency Anemia, Nitric Oxide Synthase, Nitric Oxide, Bile Supersaturation, Mentzer Index

INTRODUCTION:

The introduction of Gall Bladder disease to mankind dates back to the 21st Egyptian Dynasty (1085-945 BC), when gall stones were discovered in the mummy of priestess of Amen. Gallstone disease in India is the most common biliary pathology known, same is the case in other parts of the globe. Gallstone disease, in the absence of metabolic disorders such as hemolytic anemias, can be attributed to various etiological factors which ultimately lead to bile super saturation. Two of the major culprits are of utmost importance in the Indian subcontinent; especially the northern parts of India- high cholesterol diet and iron deficiency anemia. Both these causal factors are nutritional in origin and become altogether important in a country like India with the demographics and economics favoring extremes of nutritional status. Importance of this pathology in this very region has been supports by studies of **Tandon R. K.** who concluded that average age of patients in India is a decade younger than those in the west. Trace elements such as Iron, Copper, Zinc and even disturbances in biliary pH have been postulated to be a causal factor for gallstone disease. Several studies have propounded the theory of iron deficiency being a cause for bile super saturation and they have been supported by investigations such as serum iron values, serum ferritin values, TIBC values, bile cholesterol concentration values, etc. Iron (Fe) is a co- enzyme for the enzyme NOS (nitric oxide synthase) which catalyzes the process of local site Nitric Oxide (NO) generation. NO is an important factor for maintaining Gall Bladder tone and is thought to have effects on motility of various anatomic components of the biliary tree. This is, at present, the most feasible explanation of the mechanism of how iron deficiency can lead to bile super saturation and act as a nidus for gallstone formation.

OBJECTIVES:

1) To establish a relation between gallstone disease and iron deficiency anemia.
2) Define iron deficiency anemia based only on Complete Blood Counts (CBC) for this very purpose.
3) To look for future predictive and hopefully preventive prospects of this association.

AIM: To translate the above mentioned association from research purposes in to clinical practice without causing additional economic burden to the patient.

MATERIALS AND METHODS

The study was conducted in the department of general surgery at Indraprastha Apollo Hospitals, New Delhi from 01.08.2017 to 31.07.2018

SITE

DEPARTMENT OF GENERAL, LAPAROSCOPIC AND ROBOTIC SURGERY,INDRAPRASTHA APOLLO HOSPITALS SARITA VIHAR NEW DELHI

100 CASES AND 100 CONTROLS

CASES : Patients undergoing cholecystectomy

CONTROLS: Asymptomatic individuals presenting to the routine health check packages of the institute.

INCLUSION CRITERIA :

- Age : 21 to 80 years
- Gender : males and females both
- Residents of north india for a period of atleast 5 years.
- [NORTH INDIA- Bihar, Chandigarh, Delhi, Haryana, Himachal pradesh, Jammu and Kashmir,
- Punjab, Rajasthan, Uttarakhand and Uttar Pradesh]--as per MINISTRY OF HOME AFFAIRS
- Patients diagnosed as a case of gallstone disease by ultrasonography abdomen.
- Controls with ultrasonographic documented absence of Gallstone disease.

EXCLUSION CRITERIA:

- Patients who are known cases of hematological disorders
- Patients who are known cases of hemoglobinopathies
- Patients who are known cases of genetic and familial lipid disorders
- Residents of North Indian states who have shifted less than 5 years ago
- Patients less than 20 years and more than 80 years of age
- Patients who are diagnosed cases of malabsorption syndromes such as celiac sprue, lactose intolerance, etc.

CBC (Complete blood counts) of the cases and controls were noted. CBC performed in the institute with combination of automation + microscopy.

Ultrasonography performed on Outpatient basis by Sonologist of the designation of Senior Consultant.

REFERENCE VALUES:

1) ANEMIA :	**MALES- Hb <13g/dl**
	FEMALES- Hb <11g/dl
2) MCV (mean corpuscular volume) :	**83.0 – 101.0 fL**

3)MCH (mean corpuscular hemoglobin): 27.0 – 32.0 pg
4)MCHC (mean corpuscular hemoglobin concentration): 31.5 – 35.0 g/dl
5)RBC COUNT : 4.5 – 5.5 million/ microL

MENTZER INDEX: MCV / RBC COUNT
In cases of microcytic hypochromic anemia
- **<13 most likely of thalassemia**
- **>13 most likely of iron deficiency anemia**

STUDY DESIGN
CASE CONTROL STUDY

RESULTS:
TABLE NO. 01 :

AGE(YRS)	CASES	CONTROLS
21 – 30	08	09
31 – 40	22	26
41 – 50	26	30
51 – 60	24	21
>60	20	14

- MEAN AGE OF CASES IS **46.52 YRS**
- MEAN AGE OF CONTROLS IS **46.04 YRS**
- BOTH CASES AND CONTROLS PEAK IN THE AGE BRACKET **41 – 50 YRS**

TABLE NO. 02 :

GENDER	CASES	CONTROLS
MALES	47	49
FEMALES	53	51

- FEMALES HAVE A SLIGHT OVERALL AGE HIGH INCIDENCE OF CHOLELITHIASIS IN THE STUDY

TABLE NO. 03 :

AGE(YRS)	CASES (ANEMIC)	CASES (NON ANEMIC)	CONTROLS (ANEMIC)	CONTROLS (NON ANEMIC)
21 – 30	05	03	03	06
31 – 40	17	05	11	15
41 – 50	19	07	16	14
51 – 60	16	08	12	09
>60	14	06	06	08

PREVALENCE OF ANEMIA IN CASES ARM IS **71%**
PREVALENCE OF ANEMIA IN CONTROLS ARM IS **48%**

TABLE NO. 04 :

	CASES	CONTROLS
IDA +	71	48
IDA --	29	52

ODDS RATIO = 2.65

ATTRIBUTABLE RISK (RISK DIFFERENCE) = (71 – 48) X 100 / 71
= 32.39 (32.39 % OF COLELITHIASIS IS DUE TO IDA)

RELATIVE RISK (RISK RATIO)= 2.44 (2.44 TIMES MORE IN IDA ARM THAN IN NON IDA ARM)
CHI SQUARE = 10.976

p-value = 0.000923
CI = 0.95
Upper CI = 4.75
Lower CI = 1.48

CONCLUSION :
1) PEAK AGE BRACKET FOR CHOLELITHIASIS WAS 41 TO 50 YEARS.
2) FEMALES HAD AN OVERALL HIGHER INCIDENCE FOR CHOLELITHIASIS
3) ANEMIC INDIVIDUALS HAD A HIGHER INCIDENCE OF CHOLELITHIASIS THAN THE NON-ANEMIC ONES (p-value 0.000923)
4) ANEMC INDIVIDUALS ARE 2.44 TIMES MORE LIKELY TO DEVELOP CHOLELITHIASIS AS COMPARED TO NON-ANEMIC INDIVIDUALS

DISCUSSION :
Iron Deficiency Anemia Has Been Implicated As A Culprit In The Pathogenesis Of Cholelithiasis In Various Studies. Causal Asssociation Is Not Established But Gall Bladder Dismotility Secondary To Reduced Levels Of Nitric Oxide (no) Has Been Implicated. Various Studies Have Time And Again Proved This Association With The Help Of An Array Of Investigations. The Incidence Of Iron Deficiency Anemia And Cholelithiasis Is High In The North Indian Population And In Such Epidemiological Profile, This Association Becomes Multiplicative.

This Association Needs To Be Translated Into Clinical Practice Keeping In Mind The Economic Burden Of It. If We Investigate Further On Defining Iron Deficiency Anemia Based On Complete Blood Counts Parameters Only, It Becomes A Cost Effective Way Of Applying This Association To The North Indian Population (or Broadly Speaking The South East Asian Population For The Sake Of It) Of The Economic Strata For Which Costly Investigations Are Equivalent To Added Morbidity. Iron Deficiency Anemia Should Be Considered For Considered An Important Causal Factor For Cholelithiasis And This Association Considered For Predictive Value Or Hopefully, Preventive Value In The Future.

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