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Co-incidental urolithiasis in patients with gall stones

Dr. Safa El-dean S.Nema*

ABSTRACT

Background

Gall stones and renal stones are one of the common pathologies recorded all over the world , there are many types for both renal and gall stones as well as different etiology and causing different signs and symptoms .

Objective.

The study planned to determine if there is significant statistical association between the coexistence of renal stones with gall stones .

Patients and Methods

140 patients presented with gall stones from the period of January 2007 until march 2008 in out patient clinic, 117(83.5%) patients where females and 23(16.5%) where males, all the patients examined by ultrasound for both renal and gall stones and some patients with renal stones examined by KUB x-ray and/or IVU, records of all patients reviewed for age, gender, gross appearance of both types of stones post operatively (for those who were operated) and for those patients passing renal stones per urethra and correlated with the type of gall stone that seen post operatively, the patients underwent different modalities of treatments, by surgery (open or laparo-scopic cholecystectomy),(nephrolithotomy),or conservative for both types of stones.

Results.

Regarding the gall stones, surgical treatment done for 118 patients, 100 of them by laparoscopic cholecystectomy and open cholecystectomy for 18 patients, while 22 patients treated conservatively, and regarding the renal stones 12 patients of them operated during the course of study, and 20 patients of them passing their stones per urethra, and all these stones seen grossly, the other patients treated conservatively, the study shows positive presence of renal stones in 95 (67.9%) patients of total number, the coincidence was noticed to increase with age (p value >0.05) and with pigmented gall stones and female sex (p value <0.05 for both).

Conclusion

There is significant positive coincidental presence of renal stones in patients with gall stones in this study.

Aim of Study

This study planned to determine the statistical relation ship between coincidental presence of renal stone(s) and gall stone(s) after observing a remarkable incidental occurrence of both of them, a step that hinders the search for their etiological factors.

*M.B.CH.B. F.I.C.M.S. Assistant Professor، surgical department ،Kufa Collage of medicine

INTRODUCTION

Stones in human beings ,their complications and related diseases are one of the most common illnesses , and one of the most common types are the renal and gall stones the earliest documented case, renal stones found in 7000 years old mummy [(1)].

The other less common types of stones are the pancreatic duct stones which may be presents in chronic pancreatitis and salivary gland ductal stones (usually submandibular sialolithiasis) which are associated with chronic inflammation of salivary glands[(2,3)].

Gall stones (cholelithiasis)

Incidence

Gall stones are the most common biliary pathology, recent studies show that 10-15% of adult population in USA had gall stones(20 millions), 3% of them underwent cholecystectomy, 85% of them asymptomatic, 1-4% of them develop symptoms each year, females more affected than males 3 : 1, and first degree relatives of patients with gall stones have 2 fold greater prevalence.(autopsy reports shows prevalence of 11-36%)[(4,5)].

Types of gall stones

Cholesterol stones

most common type in western countries (80% of gall stones), either pure cholesterol (10% of gall stones) they are single and large stones, or mixed stones which cholesterol forming 70 % of their contents, and variable amounts of bile pigments and calcium, they are multiple , variable in size may be hard , faceted , white to yellow in colour, form in gall bladder. [(6,7,8,)] .

pigmented stones

20% of gall stones in western countries, dark because of the presence of calcium bilirubinate, contain 20% cholesterol.

Black pigmented stones

composed of calcium bilirubinate mixed with calcium phosphate and carbonate, They accompany haemolysis (hereditary spherocytosis, sickle cell disease, thalassaemia and prosthetic heart valves, cirrhosis), Usually multiple, black, small, brittle, irregular, some time speculated, form in gall bladder [(6.7.8.9.)].

Brown pigment stones

composed of calcium bilirubinate, calcium palmitate, calcium stearate as well as cholesterol, its less than 5% of gall stones, its rare in gall bladder, and formed in ducts, related to bile stasis and infection with bacteria like E-coli, they are brownish yellow, soft, [(6.7.8.9.)].

Etiology

Gall stones form as a result of solid setting out of solution due to

Impaired gall bladder function

due to inefficient emptying of gall bladder, absorption defects and excretion defects, these causes may aid the aggregation of nucleated cholesterol crystals(bile stasis), such as prolong fasting, total parenteral nutrition, gall bladder dyskinesia, and opiates[(4.6.7.)].

Cholesterol nucleating factors

Mucus **facilitates excretion of bile by lubrication of bile passage, and protect the gall bladder mucosa from the effect of bile to prevent ulceration and desquamation of epithelium, so if decrease in some gall bladder disease will aid gall stone formation[(4,10,11)]**

Glycoprotein **HDL is the preferred type of cholesterol for biliary secretion , so increase HDL transport to liver can also cause cholesterol**

hypersecretion in the bile lead to stone formation[10].

Infections **such as E-coli and klebsiella infections which produce *B*-glucoronidase that convert soluble conjugated bilirubin to insoluble unconjugated state lead to formation of soft earthy brown stones[6,7,8,9].**

Supersaturated bile

Age increase gall stone formation associated with increasing age especially after the age of 40 years, and the decrease in body water content (45% of body weight) may have role[ ].
Iron deficiency low serum iron levels lead to bile supersaturation with respect to cholesterol which lead to gall stone formation[13].Gender usually incidence increase in females and pregnancy, and hormones have been implicated in unproved correlation between calculi and parity, and the predominance in females[5].Genetics in pima Indians tribe 70% of females by the age of 30 years and 70% of males by the age of 60 years have gall stones. While African masai tribe on the other hand do not have gall stones[14].Obesity because cholesterol secretion is greatly increased with out any reduction in bile salt or phospholipids secretion[8,15] .Diet incidence increase in high cholesterol or fatty diet ingestion by the patients[8,15].

Entero-hepatic circulation of fatty acids

Bowel transit zone

impaired intestinal motility my facilitate gall stone formation by influencing biliary deoxycolate level or by modulating interdigestive gall bladder motility[16].

Faecal flora

by their action on conjugation of bile acids in large bowel causing reabsorption of of bile salts aid in decrease stone formation[16].

Deoxycolate

replenish bile acid pool reducing cholesterol synthesis and secretion so decrease stone formation[16].

Ileal resection

because bile salt secretion is diminished by resection of distal third of ileum due to defect entero- hepatic circulation of bile salts by decreasing its concentration lead to cholesterol stone formation[16]

Urinary stones (urolithiasis)

They are poly crystalline aggregates composed of varying amounts of crystalloid and organic matrix.[8,9].

Incidence

It's the most common urinary tract disease after the urinary tract infections, 12% of population affected in USA , recurrence rate as high as 50% with in 5-10 years, 75% with in 20 years, male to female 3:1 , White population or Caucasians affected more than Africans, peak age 30-50 years.[1].

Types of urinary stones

Calcium calculi **80-85% of renal stones are calcareous, calcium oxalate and calcium phosphate are the main types, normal calcium intake 900-1000 mg/day, one third of this calcium absorbed by small bowel (jejunum), and increase this absorption result in increase in calcium filtered through glomerulus lead to absorptive hypercalciuria . hypercalciuria of renal origin is due to an intrinsic renal tubular defect in calcium excretion.[17,18,19].**

Oxalate calculus (calcium oxalate) **oxalate is the normal waste product of metabolism and its insoluble, 10-15% of oxalate found in**

urine originate from diet. Presence of calcium in bowel lumen is an important factor in oxalate absorption amount, precursors of oxalate are glycine and ascorbic acid. Hyper oxaluria may develop in patients with inflammatory bowel disease, small bowel resection and bowel bypass, chronic diarrhea(dehydration), and steatorrhoea. Renal calculi develop in 10-15% of these patients, these cause limited amount of calcium available to bind with oxalate and remain insoluble form, rapidly absorbed and increase oxalate excretion in urine lead to urolithiasis[20,21].

Phosphate calculus (calcium phosphate) **form in alkaline urine when proteus organism present which splits urea to ammonia, may enlarge to fill all the renal collecting system to form stag horn calculus[22].**

Non-calcium calculi **15-20% of renal calculus are non calcareous.**

Struvite stone

Magnesium-Ammonium-Phosphate (MAP), form 10% of renal calculi, common in females, associated with urea splitting micro organism[ ].

Uric acid and urate stones

5-9% of all urinary calculi, usually in males, may be contaminated with calcium salts, or mixed stones of ammonium and sodium urate which is found usually in children, form due to elevated uric acid level(dehydration), excessive purine intake and endogenous uric acid production[23,24].

Cystine calculi **1% , found in patients with inborn errors of metabolism that lead to cystinuria, radiopaque due to sulpher, they are hard[25].**

Xanthine calculi **rare, secondary to congenital deficiency of xanthine oxidase[26].**

Indinavir calculi **rare, indinavir is a drug prescribed for HIV infected patients, its protease inhibitor, these stones found in 6% of patients treated by this drug.**

Very rare stones silicate **due to long term antacids treatment, triamterene associated with anti hypertension drug (dyazide)[27,28].**

Etiology

In any mineralization the crystal and matrix intertwined, stone formation requires supersaturated urine and its depend on rinary PH, ionic strength, solute concentration, complexation

Dietetic

deficiency of vitamin A cause desquamation of epithelium, the cells form around which stone is deposited, dietary imbalance show relation ship with renal stones in a study of economic conditions in a places where stone are common due to high protein diet especially the animal protein Increase salt intake (sodium) related to stone formation[29].

Altered urinary solutes and colloids **dehydration lead to increase concentration of urinary solutes and tends to cause precipitation, reduction of urinary colloids which absorb solutes or mucoproteins which chelate calcium will result in tendency for stone component to come out of solution**

Decreased urinary citrate **citrate is an important inhibitor for urinary stone disease, the presence of citrate (300-900)mg as citric acid tends to keep relatively insoluble calcium phosphate and citrate in solution. Urinary excretion of citrate is under hormonal control, and decrease in : hypokalaemia,fasting, hypomagnesaemia,androgens, gluconeogenesis,and enstruation[30,31].**

Renal infections **infection favors the formation of urinary calculi, stone formation are common when urine is**

infected with urea splitting streptococci,staphylococci,and proteus.predominant bacteria found in the nuclei of urinary stones are Staphylococci and E-coli

Inadequate urinary drainage and urinary stasis

stones are liable to form when urine dose not pass freely

Prolong immobilization

immobilization for any cause is liable to result in skeletal decalcification and increase in urinary calcium, favor formation of calcium phosphate calculi[32,33].

Hyperparathyroidism

(usually primary type) lead to hypercalcaemia and hypercalciuria, found in 5% of patients with radio opaque calculi, In case of recurrent or multiple stones, hyperparathyroidism should be excluded, 50% of patients will presents with nephrolithiasis of resorptive hypercalciuric type with great elimination of calcium in urine.

Randall[35] suggested that the initial lesion in some cases of kidney stone was an erosion at the tip of renal papilla, deposition of calcium on this erosion produce a lesion called Randall's plaque, minute concentration (microlith) regularly occur in renal parenchyma, *Carr*[36] postulated that these carried by lymphatics to the sub endothelial region and accumulate, ulceration of epithelium expose them to the urine which result in stone formation.

PATIENTS AND METHODS

This study done over the period of February 2007 till march 2008 , where 140 patients presented with gall stone(s) as an out patient , we checked for the concomitant presence of renal stones using ultrasound with probe 3.5-5 Mhz curved array transducer and some patients have KUB and /or IVU , only patients with stones more than 0.6 cm regarded as positive association. Patients operated upon checked for the type of gall stone grossly and this apply for patients with urinary tract stones in addition to those who pass the stones per urethra which also recorded . The data concerning the I.D. of the patients collected, type of surgery whether with or with out common bile duct exploration, statistical analysis done for whole data using cross sectional retrospective study and chi- square (x^2) is used for statistical analysis to fined out the significance of association .Treatments of both types of stones done by surgery(open or laparoscopic for gall stones, and open surgery for renal stones) or conservative .

RESULTS

The data collected from 140 patients, 117 (83.5%) of them were females and 23 (16.5%) were males , 118 (84%) of patients underwent cholecystectomy and 22 (15.8%) treated conservatively , of those underwent surgery 100 (84.7%) operated by laparoscopic cholecystectomy and 18 (15.5%) by open cholecystectomy with common bile duct exploration Of the total number of patients, 95 (67.9%) 0f them found to have positively associated urinary stones, and 45(32.1%) negatively associated.

71 (71%) of those underwent laparoscopic cholecystectomy were positively associated with renal stones and 29 (29%) negatively associated , from those 71 patients 66 (93%) of them have kidney stones and 5 (7%) have vesical stones .Of those underwent open surgery 10 (55.5%) found to be positively associated with urinary stones and 8 (44.5%) negatively associated .For those treated conservatively 16 (72.7%) positively associated and 6 (27.3%) negatively associated .

From the total number of females , 81 (69.2%) of them positively associated, and 36(30.8%) negatively associated. and 14 (60.8%) of males show positive association, and 9(39.2%) negatively associated.The follow up of the patients during the period of study show that Renal stones of 32 patients who where show the positive association had been seen grossly after the operation in 12 patients, and after passing per urethra in 20 patients, all these stones grossly appear as spiky, dirty, brown to black giving the appearance of calcium oxalate stones.

DISCUSSION

There was no study during our search that co relate the association between renal stones and gall stones , these two different organs may share common diseases like multicystic liver association with polycystic kidneys , bile pigment excretion in urine of patients with obstructive jaundice , in hemolytic diseases , patients may have pigmented gall stones and heamoglubinurea , glycine which is the precursor of oxalate as well as play important role in conjugation of bile acids ….. etc, the idea is that both organs are responsible for excretion of human waste products and this might be, in some how , related to the etiology of stones formation in both of them , although the factors contributing in this pathology are far from settlement.Gall stones and renal stones contain some common chemical constituents ,for example calcium , phosphate , some of micro organisms like E coli , Klebsiella , some times are inhabitants of both organs, these facts may participate in searching for the phenomenon of concomitant occurrence of both types of stones , this was supported by the statistical results obtained in this study

In this study no control group taken because the incidence of renal stones in general population is already determined (12% in USA) [(1)], and there is no statistical study showing the incidence of renal stones in the area of the study. The results show that 95 (67.9%) patients out of 140 patients with gall stones are positively associated with renal stones .The study show that their is positive association in the incidence of the renal stones and gall stones and this association was maximum at age group 45-54 years (20 patients out of 25(80%)) , after this age there is a decline in this association, while the age group of 35-44 years showing the peak age of incidence of gall stones and showing positive association of 78% and that's may be due to the number of patients presented in this age group as shown in table no.(1).With increasing age there is decrease in water contents of the body which may reach 45% of body weight this may lead to more concentrated body fluids and excretions and more deposition of solid contents of the excretions which may lead to stone nucleation and formation for both types renal and gall stones.

The study show that patients with pigmented gall stones are more positively associated with renal stones as shown in table no.(2),possibly the shared constituents play role in the occurrence of both. The study also show that the positive association more common in females than in males as shown in table no.(3) ,this is merely statically back ground as rush in chemical and hormonal analysis is mandatory to find the possible links also the relative increase in the presence of gall stones in female gender compared with the male which is in turn lead to increase the association.Desquamation of epithelium may play a role in both types of stones by the formation of a nidus where the particles can deposited and nucleated to form a stone.Type of the diet may also play a

role in the formation of both types of the stones when there is high protein and fatty meals especially of animal types, and this may be due to excessive purine regarding the formation of renal stones of urate type [24] Bacterial infections like E-Coli, may play a role in the formation of both types of stones, they produce *B*- glucoronidase that convert soluble conjugated bilirubin to insoluble unconjugated state lead to formation of gall stones, while these infections act as urea splitting organisms result in Magnesium-Ammonium-Phosphate renal calculi, also chronic pyelonephritis and ulcerative processes lead to suitable nidus for the deposition and stone formation [6,7].

CONCLUSION

The study showing significant statistical association between the incidence of both stones in the patients, his association is high with the increasing age, pigmented stones and female sex

RECOMMENDATIONS

Our study represents a primary hint for this statistical association and need further investigations and studies regarding biochemical, bacteriological, hormonal, environmental and pathological factor (hyperparathyroidism, inflammatory bowel disease, terminal ileum resection, dehydration of any cause) which may be blamed in the formation of both stones and the association between them.

By understanding the aetiology and risk factors share in the formation of both types of stones, preventive measures can be taken.

Table No. (1) show the number of patients who are positively associated with renal stone(s) in different age groups and sex .

Patients age group (years)	Patients Number (100%)	Male	Female	Number of Patients with Positive asso-ciation. (%)
15 – 24	14	5	9	6 (42%)
25 – 34	21	1	20	9 (42%)
35 – 44	50	5	45	39 (78%)
45 – 54	25	2	23	20 (80%)
55 – 64	19	4	15	13 (68.5%)
65 – 74	8	4	4	6 (75%)
75 – 84	3	2	1	2 (66.5%)
Total	140	23	117	95 (67.9%)

$X^2 = 12.24$ d.f = 6 p. value > 0.05

Table no. (2) show the types of gall stones in those who were operated whether positively or negatively associated with renal stones.

Group of Patients	Patients with Mixed stones	Patients with Pigmented stones	total
Patients who Where operated	84(100%)	34(100%)	118(100%)
Patients with Positive association Of renal stones	55(65.5%)	28(82.4%)	83(70.3%)
Patients with Negative association Of renal stones	31(34.5%)	4(17.6%)	35(29.7%)

$X^2 = 4.17$ d.f = 1 p. value <0.05

Table no.3 shows the sex of the patients with gall stones Who are positively or negatively associated with renal stones

Sex of the patients with gall stones	Positively associated with renal stones	Negatively associated with renal stones	total
Female	81 (69.2%)	36 (30.8%)	117(100%)
Male	14 (60.8%)	9 (39.2%)	23(100%)
Total	95(67.9%)	45(32.1%)	140(100%)

$X^2 = 0.38$ d.f = 2 p. value <0.05

diagram no. (1) show the no. of patients who are positively associated with renal stones in differant age groups.

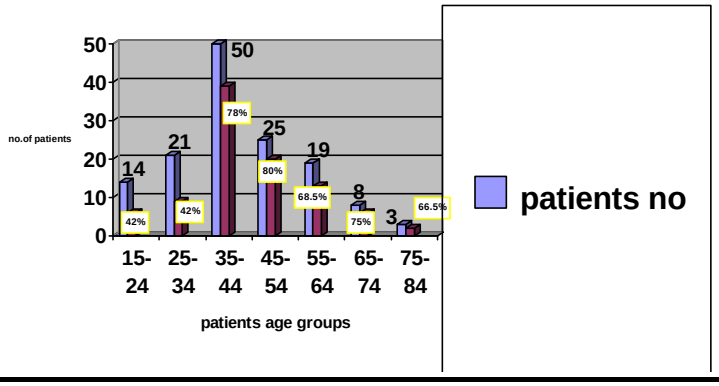


diagram no. (2) show the the types of gall stones in those who where operated whether positively or negatively

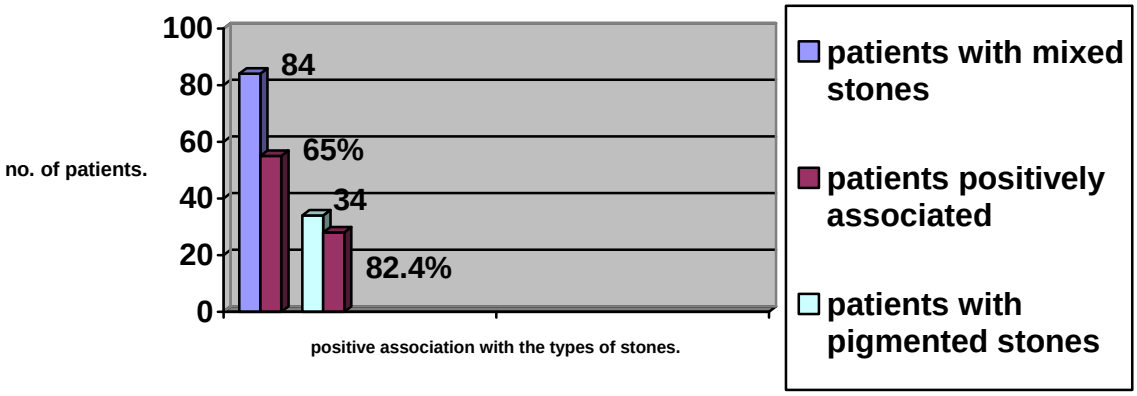
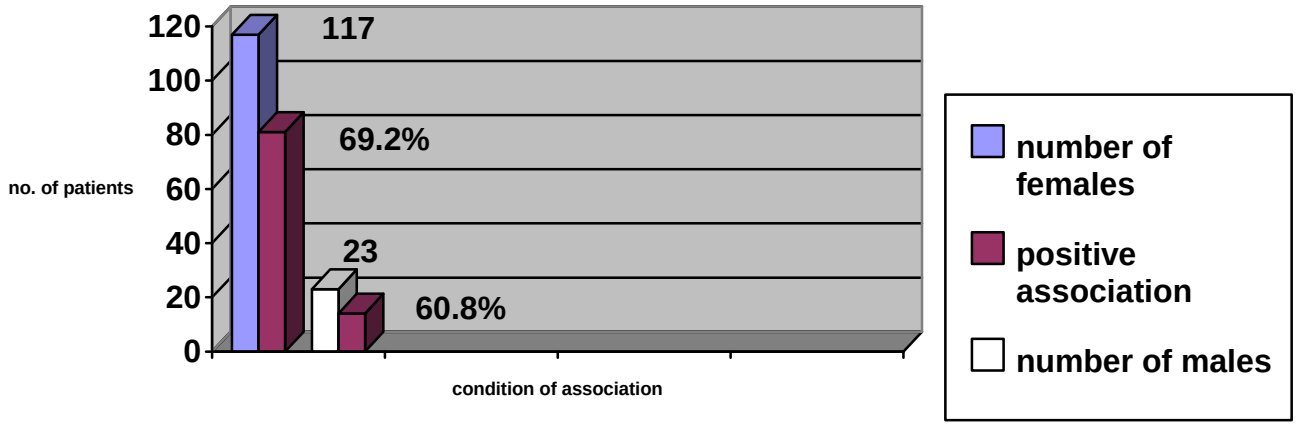
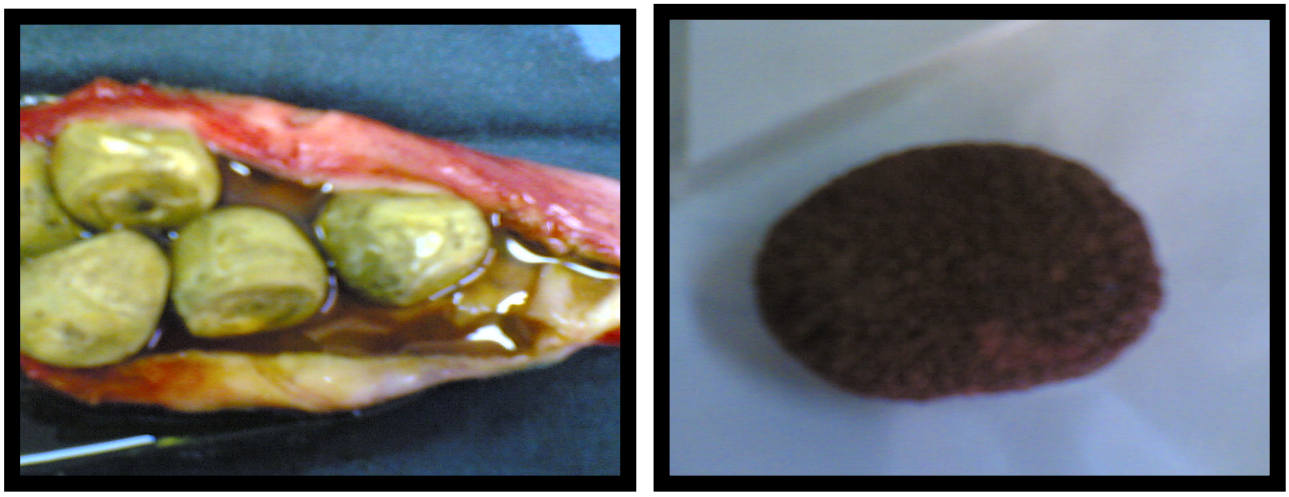


diagram no. (3) show the positively associated patients with renal stones with the type of sex





Gall stones (above) and renal stone (below) seen grossly postoperatively after laparoscopic cholecystectomy and nephrolithtomy for one of the patients in the study

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دراسة العلاقة بين حصى المسالك البولية و حصى القناة الصفراوية

د.صفاء الدين سالم البعاج
أختصا ص جراحة المجاري البولية ، كلية الطب ، جامعة الكوفة

الخلاصة

حصى المرارة والقنوات الصفراوية وحصى المسالك البولية هي من الأمراض الشائعة والمنتشرة في عموم أنحاء العالم، وهي تتكون من أنواع عديدة كما إن مسبباتها كثيرة، وتتكون نتيجة لهذه الحصى أمراض عديدة للإنسان.

هدف الدراسة

دراسة احصائيه استرجاعية لغرض إيجاد العلا قه الاحصائيه بين حصى المسالك البولية وحصى المرارة أو القناة ألصفراويه، ودراسة العلا قه ألمتوقعه (إن وجدت) في تسبب نوعي الحصى المذكورة.

المرضى وطريقة البحث

مائه وأربعون مريضآ مصابين بحصى المرارة أو القنوات الصفراوية تمت دراستهم للفترة من كانون الثاني سنة ٢٠٠٧ ولغاية آذار سنة ٢٠٠٨ في العيادة الخارجية ، ١١٧ مريضآ من الإناث و ٢٣ مريضآ من الذكور، تم فحص جميع المرضى بواسطة جهاز الأمواج فوق ألصوتيه لكلتا نوعي الحصى، كما تم إجراء الفحوصات ألشعاعيه وتلوين المسالك البولية الوريدي لبعض المرضى المصابين بحصاة الكلى،المحاور التي تم دراستها للمرضى هي العمر، الجنس، المظهر الخارجي لكلتا نوعي الحصى للمرضى الذين أجريت لهم العمليات ألجراحيه، أو المرضى الذين سقطت منهم حصى المسالك البولية من الاحليل، وتمت مقارنتها بحصى المرارة بعد ألعمليه،المرضى عولجوا بطرق متعددة، منها العملية ألجراحيه التقليدية او بواسطة المنظار، وقد اجري التحليل الاحصائي وفق الدراسة المقطعية .

النتائج

ظهرت علاقة قيمة فيما بين تواجد النوعين من الحصى في المسالك البولية و القنوات الصفراوية والمرارة ، حيث ان النسبة بلغت ٦٧,٩ % ،من خلال دراسة مائة وأربعين مريضا ومريضة . وكانت العلاقة على أشدها عند التقدم في العمر،بالأخص الفئة العمرية ٤٥-٥٤
كذلك كانت العلاقة واضحة عندما يكون نوع الحصى من المصبوغ بلون الصفراء .

التوصية

يتطلب هذا الربط الإحصائي بين نوعي الحصى إجراء المزيد من التحقق وإسناده بالتحليل الكيميائي والحياتي أو الطرق الأخرى للوقوف على المسببات للنوعين من الحصى مما يفتح الآفاق للوقاية منها .