Analysis of Cholecystectomies at Chris Hani Baragwanath Academic Hospital over three years

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine

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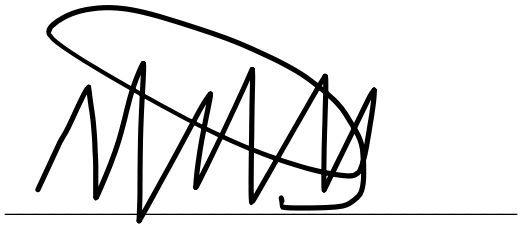
DECLARATION

I, Jean Christian Mwana Mwenyi MUSAS (Student number: 2201624), declare that this research report is my own, unaided work. It is being submitted for the Degree of Master of Medicine in Surgery at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any other degree or examination at any other University.



22nd November 2023 in Johannesburg

DEDICATION

To my wife, Lydia Lylyane Kavul Musas, we wanted to do this together, I’m glad to accomplish this to honor you.

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS STUDY

Presentations:

The preliminary data presented at the 48th Annual Meeting of the Surgical Research Society of Southern Africa, SRSSA, held in Cape Town from, 09 – 10 July 2021.

Complete work presented at the 50th Annual SRSSA Congress, 11 -12 July 2023, Durban

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LIST OF ABBREVIATIONS

CHBAH: Chris Hani Baragwanath Academic Hospital

HICs: High Income Countries

GSH: Groote Schuur Hospital

IQR: Interquartile range

LC: Laparoscopic cholecystectomy

LMICs: Low- and Middle-Income Countries

NHLS: National Health Laboratory Service

SSA: Sub-Saharan Africa

UK: United Kingdom

USA: United States of America

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ABSTRACT

Introduction

Laparoscopic cholecystectomy is a commonly performed operation globally. There has been an increasing trend noted worldwide. Reports from South African institutions are infrequent. This study aimed to analyse cholecystectomies performed in a major South African academic hospital over three years.

Materials and Methods

A retrospective analysis of cholecystectomies performed at the Chris Hani-Baragwanath Academic Hospital, CHBAH, over a 3-year period (01st January 2017- 31st December 2019) was conducted. Data was obtained from specimens sent for histology and retrieved from the National Health Laboratory database. Annual cholecystectomy rates, age and gender distribution, histological diagnosis and seasonal trends were analysed. A comparison of this data is made with previously published studies.

Results

Six hundred and forty-nine cholecystectomies were performed during the study period. Women underwent cholecystectomy more commonly than men (3.5:1; p= 0.001).

The median age of patients undergoing cholecystectomy was 42 years (IQR 29-57). There were no cases of incidental gallbladder cancer on histology. There were no significant seasonal differences during the study period. There was a fivefold increase in the annual cholecystectomy rate when compared to a previous study done at CHBAH from 1983-1985.

Conclusion

A fivefold increase was noted in the cholecystectomy rate at CHBAH when compared to previous studies. This is in keeping with international trends. This is presumably due to an increasing western lifestyle.

Keywords: cholecystectomy rate, trends of cholecystectomy,laparoscopic cholecystectomy,open cholecystectomy

1. INTRODUCTION

1.1 Background

Cholecystectomy is the removal of the gallbladder. Historically, the first case of a successful cholecystectomy was performed at Lazarus Hospital, Berlin, on July 15, 1882, by a German surgeon, Carl Johann August Langenbuch (1). On September 12, 1985, Erich Mühe, another German in Boblingen, performed the first human laparoscopic cholecystectomy (1, 2). Muhe work was disparaged and ignored (3) till Phillipe Mouret (1, 2, 4) adapted Muhe's techniques to conduct another laparoscopic cholecystectomy in France on March 17, 1987. This was rapidly adopted and became standard of care over open surgery and non-invasive gallstones therapies (5). In South Africa and perhaps the African continent, the first laparoscopic cholecystectomy was by Professor Philip Bornmann and colleagues at the Groote Schuur Hospital (GSH), Cape Town in October 1990 (6).

The introduction of laparoscopic cholecystectomy has resulted in an increase in the rate of elective cholecystectomies globally (2). There is a paucity of data on cholecystectomy rates from Sub Saharan Africa. Data from high income countries (HICs) as USA (12), Canada (23), Norway (13,16) and UK (12,14) have all demonstrated an increase in cholecystectomy rates since the advent of laparoscopic cholecystectomy. The increased cholecystectomy rates may also be in part due to increased gallstones occurrence engendered by the obesity pandemic (17). Conversely, published data of cholecystectomy rates in Sub-Saharan Africa and other LMICs remain sparse before and after the introduction of laparoscopy. A study from Nigeria demonstrated a 210 percent increase in annual cases of cholecystectomy after introduction of laparoscopic procedure between 2005 and 2015 (8). A few studies from South Africa have revealed similar trends (9-11). A Bloemfontein study reported a rate of 77.7 cholecystectomies per 100 000 admissions between 1983 and 1986 (11). In Johannesburg, a CHBAH study

showed a fourfold increase in cholecystectomy rates between 1959 and 1969. This correlated to 13.7 per 100 000 admissions for the period (9). Over two decades later, at Baragwanath Hospital again, Parekh et al reported 118 cholecystectomies performed between 1983 and 1985, giving an average of 39 patients annually (15). This rate increased in 1988 to 46 cases per annum (9).

More recently, Z Khan at al analysed 34,294 cholecystectomies and showed a female to male ratio of 5.7 with a mean age of 47.3 years (17).

Seasonal trends in cholecystectomy have been described. Chi-Mi Liu et al (20), in a review of 192,833 patients that had cholecystectomy reported more cholecystectomies in summer.

The prevalence of incidental gallbladder carcinoma has been shown to be low in various studies. In Sweden, Muszynska reported 215 cases in a review of 36,355 cholecystectomies with a 0.59 percent rate of incidental gallbladder cancer (21). A large African study reported the rate of incidental gallbladder cancer to be 0.39 percent (17).

From the experience at CHBAH over the last few years, we hypothesize that there has been an increasing trend in both open and laparoscopic cholecystectomies. This study aims to describe this patient population and report on a more recent cholecystectomy rate. A previous study (Parekh et al) at the institution allows for comparison with more recent data (15).

1.2 Objectives

Primary objectives:

- To determine the annual cholecystectomy rate at CHBAH over a three-year period between 2017 – 2019.
- To describe age and gender distributions of patients during the study period.
- To report on final histology from cholecystectomy specimens

Secondary objectives:

- To determine any variation in seasonal trends with regards to cholecystectomies during the study period.
- To compare the cholecystectomy rate at CHBAH during 2017-2019 period to previously published rates from 1983-1985.

2. METHODS

2.1 Patient selection

Data of all patients that underwent a cholecystectomy within the Department of Surgery at CHBAH, from January 2017 to December 2019 were retrieved for the study. Seasons were defined as: Spring (September to November); Summer (December to February); Autumn (March to May); and, Winter (June to August).

2.2 Data acquisition

This retrospective review was conducted with retrieved data of relevant patients from the National Health Laboratory Service (NHLS) registry reports on submitted specimens for histology. Clinical data were corroborated with hospital records and patient electronic discharge summaries.

2.3 Ethical approval

Ethics approval for the study was obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) in March 2020, followed by CHBAH Medical Advisory Committee approval. As this is a retrospective record review, no patient consent was required. Ethics clearance number: M200329.

2.4 Statistical analyses

Data were entered into an Excel spreadsheet. Descriptive statistics report means and standard deviations, or medians and interquartile ranges (IQRs), for continuous data, and frequencies and percentages for categorical data. Cholecystectomy rates were represented as the number of cholecystectomies performed in a calendar year. Statistica was used to determine the relationships between variables. To determine differences per year or per indication for cholecystectomy, the student t-test or Mann-Whitney test was used for the continuous variable

of age, and the Chi-squared or Fisher's exact test was applied, as appropriate, for categorical variables. A p value of <0.05 was considered significant.

3. RESULTS

3.1 Cholecystectomy rates:

Six hundred and forty-nine (649) patients were included in the study. The mean cholecystectomy rate over the 3-year period was 216 cholecystectomies per annum (Figure 1). In comparison to the previously published study of 1983 – 1985 form same institution, this is a 5.5-fold increase from 39 to 216 cholecystectomies per annum (Figure 2).

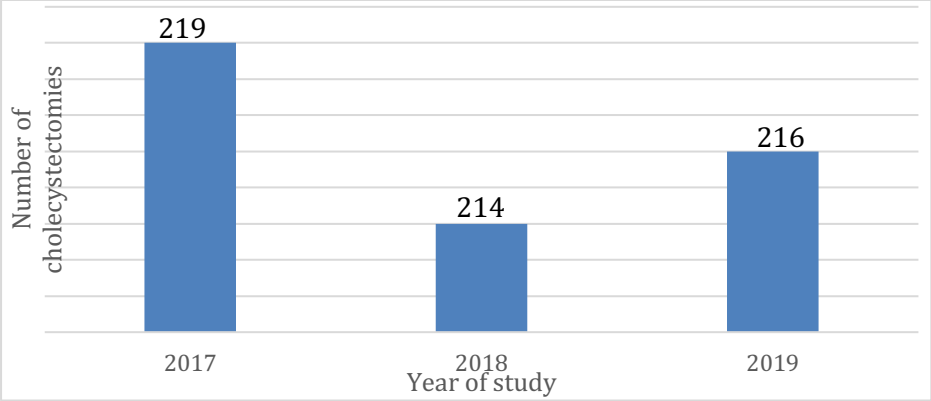

Figure 1. Cholecystectomy rates at CHBAH: 2017-2019

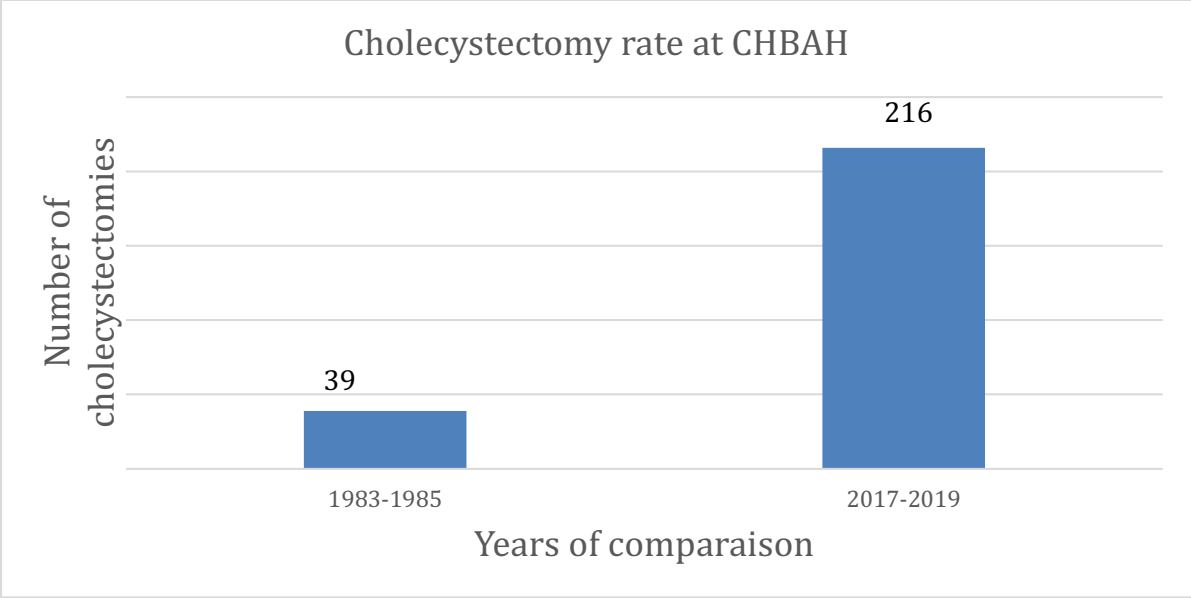

Figure 2. Comparison of mean rate of cholecystectomies per annum at CHBAH between the period 1983-1985 and 2017-2019.

Gender and age distributions

There were significantly more females (n=506, 78.0%) that underwent cholecystectomies than males (n=143, 22.0%) during the 3-year study period (p = 0.001), giving a female to male ratio of 3.5:1 as shown in Figure 3.

Overall, the patient population had a median age (IQR) of 42 (29-57) years, and this remained constant over the 3-year study period. Female patients were younger at a median (IQR) age of 41 (30-55) years when compared to male patients at 46 (27-60) years, but this did not reach statistical significance (p=0.22).

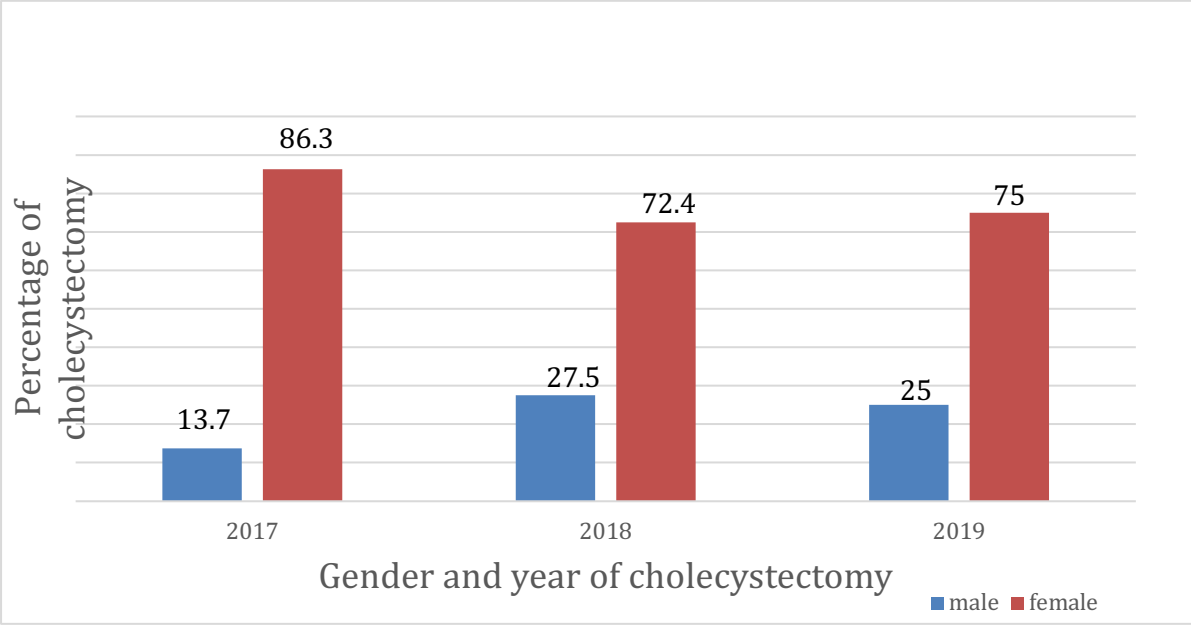

Figure 3. Percentage of cholecystectomies according to gender per annum (2017-2019)

Indications for cholecystectomy

From Figure 4, 620 cholecystectomies were performed for gallstone related disease (n=620/649, 95.5%), including acute cholecystitis, biliary colic and its complications such as choledocholithiasis. Two cholecystectomies (0.3%) were performed for trauma and 27 (4.2%), during the course of surgery for other diseases, such as pancreaticoduodenectomies, Kasai, etc. These were excluded from analysis regarding biliary disease. There were no cholecystectomies performed for gallbladder cancer.

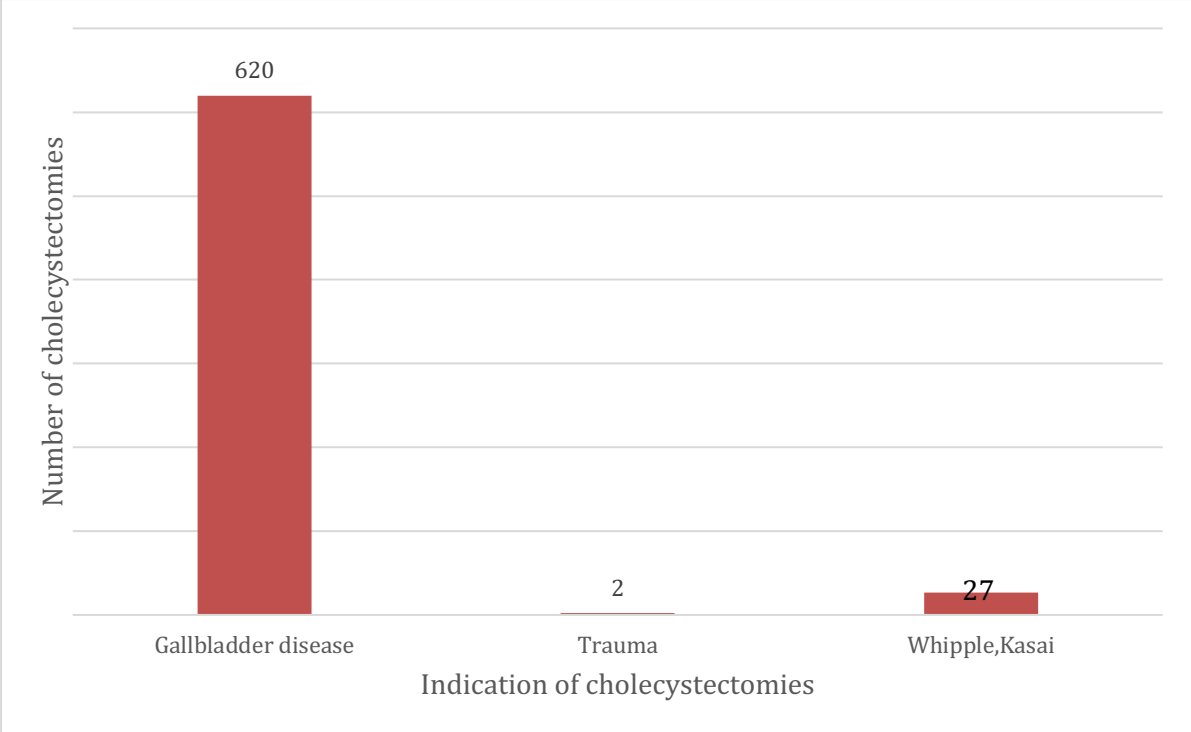

Figure 4. Indications for cholecystectomies

Histological diagnosis

Histology found inflammatory gallbladder disease, including acute and chronic cholecystitis, in 95.5% of cholecystectomies. No incidental gallbladder cancer cases were diagnosed in this study. Intraepithelial Gallbladder Neoplasia and Biliary Intraepithelial Neoplasia (BIN) type 2 were reported in two patients.

Seasonal trend

The cholecystectomies done within specific seasons are shown in Figure 5. There was no significant seasonal difference ($p=0.117$) during the study period.

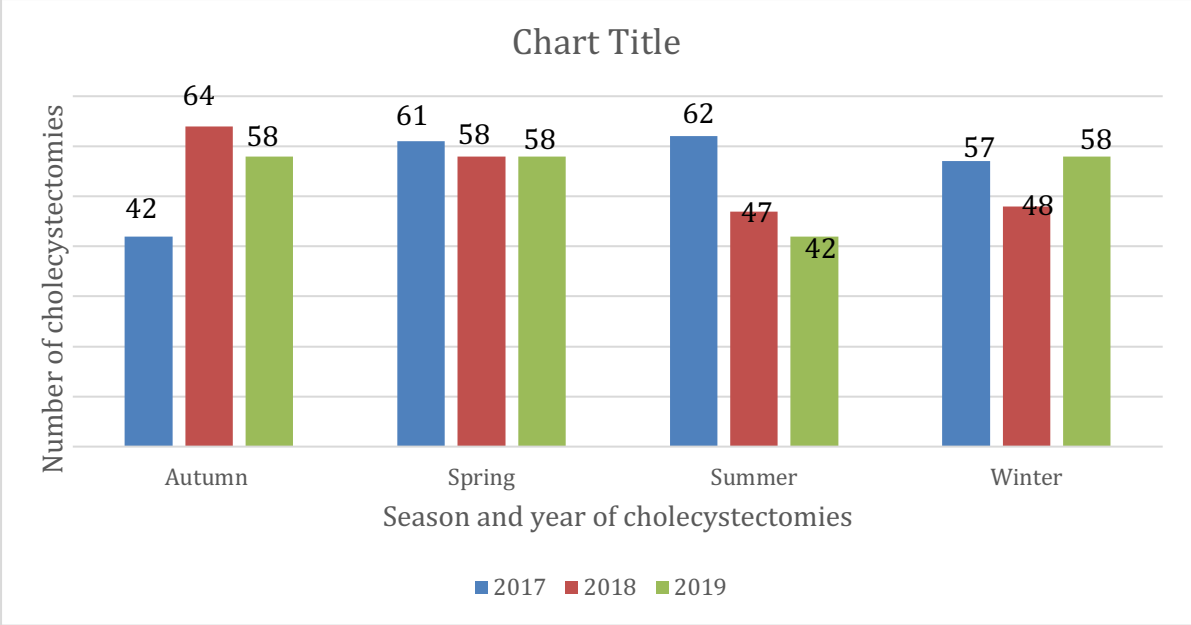

Figure 5. Number of cholecystectomies according to seasons per year of study

4. DISCUSSION

The introduction of laparoscopic cholecystectomy has resulted in an increase in the rate of elective cholecystectomies. Data from the developed world, including USA (12), Canada (23), Norway (13,16) and UK (12,14) have all demonstrated an increase in cholecystectomy rates following the advent of laparoscopic cholecystectomy. This study found a rate of 216 cholecystectomies per annum, five times the rate of cholecystectomy at the same institution just over three decades earlier (15). This supports a similar upward trend reported in the 2015 Nigerian study, albeit at a much lower rate of 3.1 cases per annum (8). The possible reasons for such an increased rate could be an increasing exposure to a Western lifestyle characterized by increased consumption of saturated fat with a decreased fiber intake as demonstrated in a previous review (17). As a result, there may be an increase in gallstone related disease in the population under study. In addition, increased access to medical care by a previously disadvantaged population may account for the increased cholecystectomy rate. Lastly, the lower threshold for surgery and enthusiasm associated with the advent of less morbid and better tolerated laparoscopic surgical procedures has to be considered as a cause for such an increase.

The age and sex distribution of patients undergoing cholecystectomies were investigated in this study. A median age of 42 years was observed. This is in line with other studies reporting that cholecystectomies are performed mostly in younger patients (16). Also an increased female to male ratio of 3.2 was noted, again in line with other studies demonstrating that females undergo cholecystectomies more often than males.

The Society of American Gastrointestinal and Endoscopic Surgeons guidelines for the clinical application of laparoscopic biliary tract surgery indicates that conditions requiring cholecystectomy include, but are not limited to, cholelithiasis (when symptomatic), choledocholithiasis, biliary dyskinesia, porcelain gallbladder, acute cholecystitis and

pancreatitis related to common bile duct stones (18). In the current study, 95.5% of cholecystectomies were performed for gallstone related disease. This corroborates findings from a 2018 study from a rural regional referral hospital in Kwazulu-Natal, South Africa, that reported biliary colic as the leading cause for cholecystectomy (19).

Although temperature was thought to be the most important variable among the relevant meteorological factors leading to development of gall bladder disease (dehydration and good environment for organisms to multiply) (20), there was no significant seasonal differences in cholecystectomy rate in this study.

Similarly, no cases of gallbladder cancer in this study, however intraepithelial gallbladder neoplasia and biliary intraepithelial neoplasia (BIN) type 2 were reported in two patients. These results would be in keeping with previous studies (17). Given the low incidence of incidental gallbladder cancer, it is not unexpected that no cases of overt cancer were found.

Limitations of this current study include the retrospective nature, which is biased by patient selection and missing data. In addition, not all cholecystectomies may have been captured in this study as only specimens sent for histology were included for analysis. However, it is common practice in the institution to send all cholecystectomy specimens for histology. With regards to changes in cholecystectomy rates, it is possible that the introduction of laparoscopic cholecystectomy as well as better access to health care may have contributed to increasing the rate of cholecystectomy as opposed to changes in the incidence of gallstone disease (17).

5. CONCLUSION

This study reports that females in their early forties were mainly undergoing cholecystectomies for gallstone related disease. Also, a fivefold increase in the rates of cholecystectomies for gallstone related disease performed at an urban South African hospital when compared to over 30 years ago was documented. The increased rate is likely to be multifactorial and may be related to disease prevalence, access to health care and introduction to laparoscopy.

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APPENDIX 1: Approved Protocol

MMed Research PROTOCOL

Analysis of Cholecystectomies at Chris Hani Baragwanath Academic Hospital over three years

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Introduction and Literature review:

Cholecystectomy is the removal of the gallbladder. Historically, the first case of a successful cholecystectomy was performed in 1878 by a German surgeon Carl Johann August Langenbuch. In 1985 Erich Mühe of Germany performed the first human laparoscopic cholecystectomy (1). Until this pivotal point, cholecystectomy was performed mainly through open surgery. In September 1992 however, the National Institute of Health consensus conference held in Bethesda concluded that laparoscopic cholecystectomy was the treatment of choice for gallbladder lithiasis (21). The Society of American Gastrointestinal and Endoscopic Surgeons guidelines for the clinical application of laparoscopic biliary tract surgery indicate that conditions requiring cholecystectomy include, but are not limited to, cholelithiasis (when symptomatic), choledocholithiasis, biliary dyskinesia, porcelain gallbladder, acute cholecystitis and pancreatitis related to common bile duct stones (17). In the USA, the indications for cholecystectomy in asymptomatic cholelithiasis include patients with large gallstones (>2.5cm), congenital hemolytic anemia and non-functioning gallbladders (22) . In Kwazulu-Natal, South Africa, Balasubramanian at al showed that biliary colic was the leading cause for cholecystectomy. In this study, females were more affected than the males (18).

The introduction of laparoscopic cholecystectomy has resulted in an increase in the rate of elective cholecystectomies. According to Pulvirenti *et al* , laparoscopic cholecystectomy has increased during the recent years and several studies from around the world have demonstrated increases (2). In Maryland, USA, the rate of cholecystectomy rose from 1.69 per 1000 patients in 1985-1987 to 2.17 per 1000 patients in 1992, an increase of 28%(7). In Ontario, Canada, the adjusted annual rate of elective cholecystectomy per 1000 population increased by 24% from 2.01 in 1988-1990 to 2.60 in 1992-2000 (23). In Norway, the cholecystectomy rate increased from 0.62 per 1000 person-years in 1990-1992 to 0.8 per 1000 in 1993-1997 and 1

per 1000 in 1998-2003 (15). In England, the rate of cholecystectomy rose to 1,4 per 1000, a 14.6% increase from 2000 to 2009(10).

There is a paucity of data on trends in cholecystectomy rates from African countries. In a single centre study from Nigeria, 173 cholecystectomies were performed between January 2005 and December 2015, with the annual number in 2005 of 7 cholecystectomies increasing to 31 cholecystectomies 2015. This corresponded to 2.7% of total elective major general surgery procedures in 2005 compare and to 9.1% in 2015. Moreover, there was an inverse relationship in the trend of laparoscopic cholecystectomy to open cholecystectomy between 2008 and 2015(11). Despite the advent of Laparoscopic Common Bile Exploration and Endoscopic Retrograde Cholangiopancreatography for the management of gallstone disease, cholecystectomy rates remain to be on an upward trend (22).

Few studies have described the experience from South Africa. Pelonomi Hospital in Bloemfontein reported a rate of 77.7 cholecystectomies per 100 000 admissions between 1983 and 1986 (13). The first studies from Chris Hani Baragwanath Academic Hospital (CHBAH) demonstrated a fourfold increase in cholecystectomy rate between 1959 and 1969. The rate was 13.7 per 100 000 admissions for this study period (13). Over two decades later, Parekh *et al* (1987) reported 118 cholecystectomies were performed in 1983-1985, giving an average of 39 patients annually (12). This rate increased in 1988 to 46 patients (13).

The age and gender distribution of patients undergoing cholecystectomies are well documented. In Norway, cholecystectomy for gallstone colic was more often carried out on younger patients, whereas older age groups were operated more for acute or chronic cholecystitis (15). Similarly, a study from Sweden in 2016 reported that in older age groups cholecystectomies were performed for cholecystitis, pancreatitis and gallstone complications (14). In addition, the mean age for cholecystectomy is also decreasing; Talseth's group from Norway reported a reduction in mean age from 56 to 51 years (15).

Females undergo cholecystectomies more often than males, often making up more than two-thirds of the operated patient population (15). On average, females are also approximately 10 years younger at cholecystectomy (15).

Laparoscopic cholecystectomy has a low complication rate with excellent recovery and return-to-work times. The most common systemic complications are pulmonary in nature, specifically atelectasis, i.e. complete or partial collapse of the lung, which can be prevented by early mobilization(17). Complications specifically related to the surgical procedure include bleeding, bile leaks. Contraindications include generalized peritonitis, cholangitis, concomitant diseases that prevent use of general aneasthetic and the patient's refusal to open cholecystectomy should urgent conversion be required (17).

The increase in laparoscopic cholecystectomies may be due to patient demand and the benefits of limited access surgery as well as the need for practice by inexperienced doctors. It is possible that an increase in laparoscopic procedures could result in an increase in bile duct injuries and other complications. In a retrospective study at Addington Hospital in South Africa, 16% of laparoscopic cholecystectomies were found to have complication, with bile duct injuries accounting for most(24). Local specialist surgeons, suggest that a bile duct injury registry needs to be established in South Africa to quantify the extent of this complication.(25)

Hypothesis

There is an increasing trend in cholecystectomies at Chris Hani Baragwanath Academic Hospital (CHBAH).

Aim and Objectives:

Aim: Analysis of current rate of cholecystectomies at CHBAH in comparison to previously published data

Primary objectives:

- To determine the annual cholecystectomy rate over a three year study period (2017 – 2019), and report on any seasonal trends.
- To determine the annual age and gender distributions of patients during the study period.
- To determine and report on the diagnosis in patients from final histology.

Secondary objective:

- To compare the cholecystectomy rate at CHBAH during our study period (2017-2019) to previously published rates during 1959-1969 and 1983-1985 at CHBAH.

Methodology

This study will be a retrospective review of patients who underwent cholecystectomies at CHBAH from 2017 to 2019. The data will be obtained from the NHLS registry's reports on submitted specimens and final histology on these patients.

Inclusion criteria:

All patients that underwent a cholecystectomy at the Department of Surgery, CHBAH, from 2017 to 2019.

Exclusion criteria

None. All specimens submitted at NHLS will be analysed.

Sample size

From the previous studies at CHBAH (2,3), the increase in number of cholecystectomies per annum was 6%, from 39 in 1985 to 46 in 1988. Considering a minimum increase of 3% per annum from 1988, this extrapolates to an estimated 101 cholecystectomies being performed per annum by 2018. Based on the even higher number of cholecystectomies per annum currently being done at CHBAH of 150-200 patients on average, an estimated total sample size to of between 450 and 550 over the three year period will be adequate. Conservatively, to detect a 3% increase per annum during the study period with a significance level (alpha) of 0.05 and power of 90% for a two sample t-test (with a standard deviation of 5 procedures), a minimum sample size of 60 cholecystectomies per annum will be sufficient. Moreover, to detect a 5-year mean difference in age between genders (with a standard deviation of 5 years), with a significance level (alpha) of 0.05 and power of 90%, a minimum number of 23 cholecystectomies per gender per annum is required. Thus, our study would be sufficiently powered.

Data analysis

Data will be entered into an Excel spreadsheet. Statistica or STATA will be used to determine any relationships between variables. The student t-test or Mann-Whitney test will be used to determine statistical associations between continuous variables, and the Chi-squared or Fisher's exact test will be used to determine associations between categorical variables and to compare with previous published reports. A p value of <0.05 will be considered significant.

Ethics

Approval will be sought from the University of Witwatersrand Human Research Ethics Committee (Medical) in March 2020, followed by hospital CEO approval. As this is a retrospective record review, no patient consent is required.

Budget/funding

None

Limitations

- The retrospective nature of the study may results in missing data points.
- The data originating from NHLS, it will be difficult to differentiate between laparoscopic and open cholecystectomy.

Outcomes and benefits

This study will document recent cholecystectomy rates from CHBAH to date. The findings of this study will serve as a reference, to determine the cause of possible increasing cholecystectomy rates in a follow up study.

Timeline

October 2019	**November 2019**	**March 2020**	**April-June 2020**	**July-August 2020**	**September-November 2020**	**December 2020**
Submission	Protocol assessment					
		HREC Approval				
			Data Collection			
				Data Analysis		
					Writing	
						Publication & Examination

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APPENDIX 2: Datasheet

Study Number	Year of operation	Gender of the patient	Age of the patient	Diagnosis from Histology	Comments

APPENDIX 3: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr JCM Musas

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200329

NAME: (Principal Investigator)	Dr JCM Musas
DEPARTMENT:	School of Clinical Medicine Department of Sugery Medical School University
PROJECT TITLE:	Analysis of cholecystectomies at Chris Hani Baragwanath Academic Hospital over three years
DATE CONSIDERED:	2020/03/27
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr O Jones and Professor D Kruger
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/07/13

This clearance certificate is valid for 5 years from the date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **March** and will therefore reports and re-certification will be due early in the month of **March** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____