

Gender Differences in Gastrointestinal, Hepatobiliary and Pancreatic Surgery and Perceived Relevance on Outcomes

—A Single Center 22-Year Observational Study in India (1996-2018)

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Abstract

Introduction: Gender differences are still quite prevalent in the present time. Although there is literature regarding gender differences in healthcare expenditure in India, there is no data regarding gender differences in hospital stay, hospital seeking behaviors and mortality. **Aim:** To evaluate the Gender differences in a hospital seeking behavior, mortality and hospital stay. **Methods:** We prospectively analyzed, from a retrospective database, all patients who underwent surgical gastrointestinal, hepato-biliary, pancreatic and splenic surgeries from 1996 to 2018 in our unit. Patients were divided into groups based on gender, admission time period and priority of admission *i.e.*, elective or emergency. Both the gender groups were compared with respect to total procedures done, hospital stay and mortality. Organ specific mortality was calculated as proportions, was analyzed and compared between the groups. Time trends of the same were observed and compared. **Results:** Of 12,411 patients, 7979 (64.3%) were males and 4432 (35.7%) were females. 9191 (74.1%) patients underwent elective procedures whereas 3220 (25.9%) had emergency procedures (**p ≤ 0.001**). Overall mortality was higher in males (n = 473, 5.92%) in comparison to females (n = 185, 4.17%) (**p ≤ 0.001**). Majority of surgeries in males were of small intestine (22.5%) in which small bowel resection was most commonly done (5.4%), whereas, gallbladder and biliary surgeries (27.4%) were the most common in females in which laparoscopic cholecystectomy was most commonly done (5.8%). Median hospital stay was higher in males (10 days vs 9 days), (**p ≤ 0.001**). Mortality was higher in females in all organ categories except in liver (6.34% vs 2.7%), pancreas (37.3% Vs 18.3%) and spleen (3.38% Vs 1.62%) where mortality was higher for male gender. Highest mortality for females was in small intestinal surgery

(34%) and for males, it was pancreatic surgery (37.3%). Highest mortality in males was emergency open pancreatic necrosectomy (21.6%) and that in females was emergency small intestinal surgery (11.9%). Although the number of surgeries in females increased over time (380 in 1996-1999 Vs 951 in 2016-2018), the proportion remained constant (36.3% Vs 38.3% in 1996-1999 and 2016-2018 respectively). **Conclusion:** We conclude that mortality is found to be higher in males after gastrointestinal surgery, which may be explained by the fact that hospital seeking behavior is more in males though it is fairly increasing in females in the recent years.

Keywords

Gender Differences, Gastrointestinal Surgery, Hepatobiliary and Pancreatic Surgery, Time Trends, Hospital Seeking Behavior, Mortality, Hospital Stay, Outcomes

1. Introduction

Gender can be defined as “an array of socially constructed roles and relationships, personality traits, attitudes, behavior, values, relative power and influence that society ascribes to the two sexes on a differential basis. It is relational, because gender roles and characteristics do not exist in isolation, but are defined in relation to one another or through the relationships between women and men, girls and boys” [1].

Simply put, sex refers to biological differences and gender refers to social differences. In comparison, the average life expectancy is shorter for men than for women in almost all countries, but the magnitude of this advantage varies geographically and historically. This highlights the importance of understanding what causes gender differences in health. Although biological factors [2] and health behavior [3] may provide a partial explanation, it is very widely assumed that men and women have a different propensity to consult healthcare providers [4] and that this may be an important contributor to the gender gap in mortality [5]. However, many large-scale studies based on survey data have now reported greater use of primary healthcare services in women in western countries [4] [6].

Gender inequalities in one form or another, with considerable contextual differences, are ubiquitous and all-pervasive in South Asia. These are manifested as differences in mortality (observed by overall sex-ratio) medically. This is the observation seen in almost every country in this region. India is no exception in this regard.

Households and communities in India often place women in subordinate positions to men [7] [8]. In healthcare, girls are frequently neglected during the care-seeking process, and they experience relatively poorer nutrition, greater delays in receiving care, and lower access to preventative and curative care [9] [10].

Biologically, it has been observed in various recent studies that those of the female sex have a better mechanism of fighting stress than males most probably

because of the influence of oestrogen on various aspects of the immune system. In most of these studies, males had a higher mortality rate compared to females. A recent review of the National Trauma Data Bank found that men were 14% more likely to die during their admission following a traumatic incident than women, a trend that was present from hospital day 1 and increased as length of stay increased [11].

A similar trend was seen in patients having traumatic brain injuries, where females showed a significantly lower mortality and rate of complications [12]. This gender disparity is also thought to be the result of the effects of oestrogen. Women under the age of 50 years, presumed to be premenopausal, had half the risk of death as age-matched men who had suffered from blunt trauma [13]. When adjusted for injury severity, these results persisted, and women still had a lower risk of mortality after traumatic injury and were also less likely to develop life-threatening complications [14].

The effects of oestrogen on different organs appears to be mediated by different receptors; oestrogen receptor-a mediates its effects on the Kupffer cells, alveolar and splenic macrophages, splenic T cells, and the small intestine, whereas oestrogen receptor-b mediates its effects on the heart, as well as the lung and small intestine [15]. This occurs through both a genomic, transcription-dependent mechanism as well as a non-genomic phosphorylation-dependent mechanism [16].

Gap in Knowledge

Though there are many studies in the literature showing gender differences in the incidence of and in seeking health care in medical gastrointestinal (GI) disease, there is a paucity of data and literature in surgical GI diseases especially in the Indian subcontinent in the emergency and elective settings.

Our aim was to study gender differences in the mortality rate and duration of hospital stay and their trends since the inception of our department in 1996 until the end of 2018, just over two decades, and also to assess how hospital seeking behavior of males and females might have influenced these variables.

2. Patients and Methods

We analysed retrospectively, prospectively collected data of patients who had been admitted to our Department of Surgical Gastroenterology and Liver Transplantation in Sir Ganga Ram Hospital, New Delhi during the study period from 1996 to 2018. Patients undergoing major gastrointestinal surgery were identified by the ICD-9 procedure codes *i.e.* oesophageal (42.4), gastric (43.5 - 43.9), small intestine (45.6), large intestine (45.7 - 45.8 and 17.3), rectal (48.4 - 48.6), hepatic (50.2 - 50.3), biliary (51.3 and 51.6), and pancreatic (52.5 - 52.7) [17].

Inclusion criteria

We included all patients who underwent surgical procedures in the emergency and elective settings.

Exclusion criteria

All patients with incomplete in-hospital data were excluded from the study.

Outcomes measured

The primary outcome measured was gender difference in mortality and the secondary outcomes analyzed were gender differences in priority and types of operations done and organ systems involved, in-hospital stay and time trends in disease presentations. Patient demographic data, hospital stay, type of operation performed, post-operative morbidities, mortality and the time period were used as variables for analysis of outcomes.

Statistical analysis

This was done using SPSS 25.0 version software. Continuous data were summarized as means with standard deviations or medians with inter quartile ranges. Categorical data were summarized as frequency with percentages and analyzed using chi-square/Fisher's exact test. Comparison of continuous data was done using the Mann-Whitney U test. For all tests a p value < 0.05 was considered to be statistically significant.

Bivariate analysis was performed for categorical dependent variables (death), and t-tests for continuous dependent variables (length of hospital stay). Multivariate analysis was performed using logistic regression for the primary and secondary outcomes.

3. Results

During the study period (1996 to 2018) a total of 12,411 patients underwent gastrointestinal, pancreatic and hepatobiliary procedures. They were divided into two groups based on gender and these two groups were found to be similar in age ($p = 0.616$) and co-morbidities. The number of gastrointestinal operations performed increased gradually over the years, but the time trends were similar in both groups. Although the number of operations in females increased over time (from 380 in 1996-1999 to 951 in 2016-2018) the proportion, when compared to males, remained constant (36.3% in 1996-1999 vs 38.3% 2016-2018). The demographic data are summarized in **Table 1** and the time trends depicted in **Figure 1**. The time trends in gender differences are depicted in **Table 2**.

A total of 9191 (74%) patients underwent elective and 3220 (26%) had emergency procedures ($p < 0.001$). The number of males undergoing both elective and emergency procedures surpassed females by a wide margin ($p < 0.001$) - 5694 (62%) males and 3497 (38%) females undergoing elective and 2285 (71%) males and 935 (29%) females emergency operations. However, the proportion of females undergoing emergency operations was significantly less than that for males (21% vs. 29%) ($p < 0.001$). The measured differences in gender among the elective and emergency procedures are depicted in **Table 3**.

Table 4 displays the breakdown by the type of procedure that patients underwent. The most common procedure done in both males and females and in total (22%, $n = 2748$) was small intestinal followed by pancreatic (15%), colonic (14%) and gall bladder (12%) operations. While the largest number of procedures performed in males were on the small intestine (23%) in females the main procedures were on the gall bladder and biliary tract (27%) with small bowel resection being the most commonly performed (5.4%) in males and laparoscopic chole-

cystectomy in females (5.8%). Males underwent a higher proportion of duodenal, gastric, anal and pancreatic procedures compared to females while biliary and gall bladder surgeries were proportionately higher in females. Both sexes underwent equal proportions of colorectal, anal, oesophageal, small intestinal, splenic, liver and portal hypertension operations.

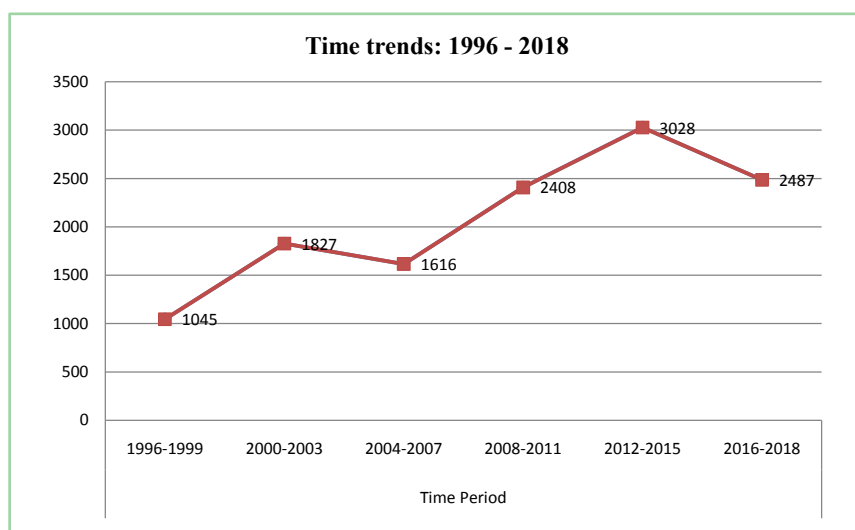


Figure 1. Total gastrointestinal surgery cases, time trends: 1996-2018.

Table 1. Demographics of men and women who underwent gastrointestinal surgery in SGRH from 1996 to 2018.

Demographics			
Gender	Male		
	Male	7979	64.3%
Gender	Female		
	Female	4432	35.7%
Age (years)	Mean	Males	48.0
		Females	48.1
Hospital stay (days)	Mean	Males	11.8
		Females	10.3
Priority	Elective		
	Elective	9191	74%
Priority	Emergency		
	Emergency	3220	26%
Mortality	Absent		
	Absent	11,753	95%
Mortality	Present		
	Present	658	5.3%
Time Period	1996-1999		
	1996-1999	1045	8.4%
	2000-2003		
	2000-2003	1827	15%
	2004-2007		
	2004-2007	1616	13%
Time Period	2008-2011		
	2008-2011	2408	19%
Time Period	2012-2015		
	2012-2015	3028	24%
Time Period	2016-2018		
	2016-2018	2487	20%

Table 2. Time trends in Gender difference.

Time Period	Gender				Total
	Male	Percentage	Female	Percentage	
1996-1999	665	64%	380	36%	1045
2000-2003	1173	64%	654	36%	1827
2004-2007	1052	65%	564	35%	1616
2008-2011	1602	67%	806	34%	2408
2012-2015	1951	64%	1077	36%	3028
2016-2018	1536	62%	951	38%	2487
Total	7979	64%	4432	36%	12,411

Table 3. Priority: Gender differences.

Priority	Gender		Total
	Male	Female	
Elective	5694	3497	9191
Emergency	2285	935	3220
Total	7979	4432	12,411

Table 4. Operation category: Gender differences.

Operation Category	Gender				Total		P value
	Male		Female		n	%	
	n	%	n	%			
Anal operations	413	5.2%	115	2.6%	528	4.3%	<0.001
Appendix Operations.	142	1.8%	74	1.7%	216	1.7%	0.652
Biliary Operations	421	5.3%	419	9.5%	840	6.8%	<0.001
Colonic Operations	1110	14%	605	14%	1715	14%	0.689
Duodenal Operations	177	2.2%	73	1.6%	250	2.0%	0.03
Gall Bladder Operations	671	8.4%	798	18%	1469	12%	<0.001
Gastric Operations	577	7.2%	250	5.6%	827	6.7%	<0.001
Liver operations	413	5.2%	206	4.6%	619	5.0%	0.197
Oesophagus Operations	210	2.6%	118	2.7%	328	2.6%	0.920
Pancreatic Operations	1394	18%	449	10%	1843	15%	<0.001
Portal Hypertension Operations	187	2.3%	105	2.4%	292	2.4%	0.928
Rectal operations	397	5.0%	245	5.5%	642	5.2%	0.184
Small Bowel Operations	1802	22.6%	946	21.3%	2748	22.1%	0.112
Splenic Operations	65	0.8%	29	0.7%	94	0.8%	0.322
Total	7979	100%	4432	100.0%	12,411	100.0%	

Females had a shorter mean duration of hospital stay of 10.3 days vs. 11.8 days in males. Their mortality was also lower (**Table 5**). Whilst the overall surgical mortality was 658/12411 (5.3%) among the study population the proportion of deaths was higher in males (5.9% males vs 4.2% in females; $p < 0.001$). There was no significant difference in mortality rates between males and females in either elective (2.6% vs. 2.1%; $p = 0.204$) or emergency (14% vs. 12%; $p = 0.056$) procedures. As expected, emergency operations had significantly higher mortality rates compared to elective procedures (14% vs. 2.4%; $p < 0.001$)

When the mortality rates in operations on the different organ systems were analyzed it was observed that females had higher death rates in all organ categories except in liver (6.3% vs 2.7%), pancreas (37% Vs 18%) and spleen (3.4% vs 1.6%) procedures where the mortality was higher in males. However, this difference in mortality rates was significant only in females in the liver and pancreas categories ($p = 0.014$ and $p = 0.003$ respectively). The highest mortality for females was in small intestinal surgery (34%) and for males it was pancreatic surgery (37%). Highest mortality in males was emergency open pancreatic necrosectomy (22%) and that in females was emergency small intestinal surgery (12%). These statistics have been clearly depicted in **Table 6** and **Figure 2**.

Table 5. Mortality: Gender differences.

Mortality	Gender		Total
	Male	Female	
Absent	7506	4247	11,753
Present	473	185	658
Total	7979	4432	12,411

Table 6. Gender differences in mortality rates among different organ systems.

Organ System	Mortality				P value
	Gender				
	Male		Female		
	n	%	n	%	
Colon & Appendix	62	13%	27	15%	0.327
Duodenum	20	4.2%	13	7.0%	0.168
Gall Bladder & Bile Duct	14	3.0%	19	10%	0.575
Liver Non-Transplant	30	6.3%	5	2.7%	0.014
Oesophagus	8	1.7%	5	2.7%	0.849
Pancreas	178	38%	34	18%	0.003
Rectum & Anal Canal	8	1.7%	4	2.2%	0.849
Small Intestine	114	24%	63	34%	0.728
Spleen & PHT	16	3.4%	3	1.6%	0.075
Stomach	23	4.9%	12	6.5%	0.596

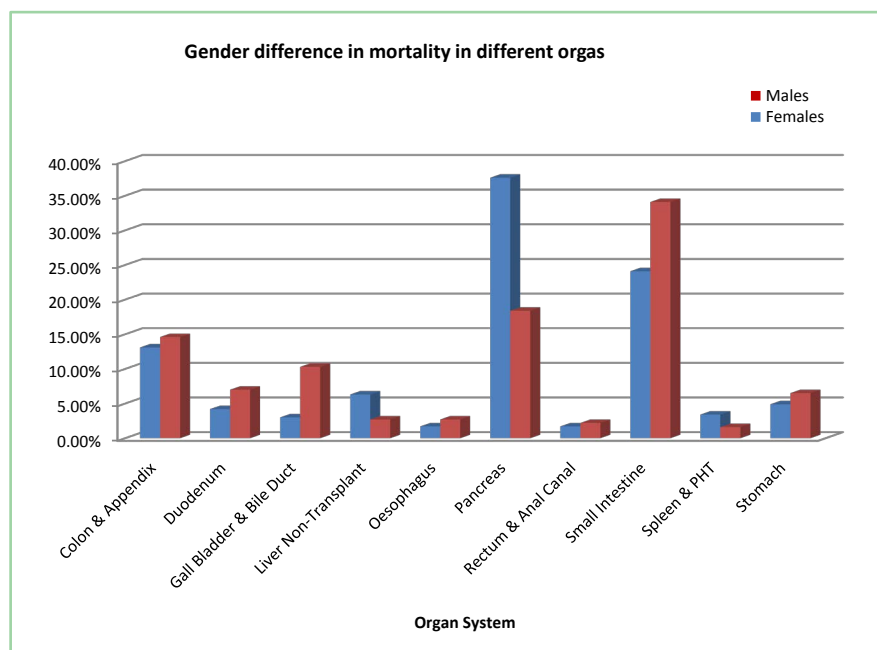


Figure 2. Gender difference in mortality rates among different organs.

4. Discussion

We found that after GI surgical procedures females fared better than males with respect to overall mortality and hospital stay. But the difference in mortality rates among the two genders was not as significant as was found in other studies from the developed countries. Though statistically insignificant females in this study in fact had higher mortality rates than males when mortality rates after operations done on most of the different organ systems was considered. Females fared better than males only in the liver, pancreas and spleen organ systems categories.

It has been established through previous studies that gender and health are related in many different ways [18] [19] [20]. This also holds good when comparing the health seeking inclination of men and women. These differences depend on various facts like inter-gender relations, cultural notions and gendered differences in access to health care [21]. Studies from across the globe show that these differences change from region to region influenced by factors like power relations [22], structural positions [23], culturally prescribed gender roles [24] or economic factors apart from cultural context. Despite the interest in gender in other areas, there is a paucity of studies evaluating how gender may affect outcomes after gastrointestinal surgery. Among the few studies conducted, the conclusions vary mainly based on whether the study population is from developing or developed countries.

While most western studies found a higher hospital seeking behavior among females with women more likely to be having their operations performed in a teaching facility than men [17], the reverse is true in most studies from developing countries like India. Even in the present study, the number of females ad-

mitted for gastrointestinal operations were about half the number of male patients admitted for the same procedures (36% vs. 64%).

According to some previous studies females from developing countries seek formal health care less than men [25] and prefer traditional healing options over them [26]. Harrison and colleagues [27], concluded in their study that, the gender socialization process, shaped by the socio-cultural ethos, also tends to impact health related notions and habits, including decisions regarding when and where to seek medical help.

According to another study by Valssof [28] the inferior status of women in a family or society also affects their decision-making regarding access to health care, education and economic resources. This is more pronounced in countries or communities with these kinds of structural restraints [29]. For example, in a study done in rural parts of Uttar Pradesh, Pune and West Bengal, it was found that health care for boys is traditionally given higher preference than health care for girls, in terms of money spent and accessing better health centers even if they need to travel greater distances to reach them [9] [30] [31].

A few recent studies however have shown that there is a slight decline in these gender differences in the recent years, with both men and women making almost similar use of formal and informal care [32]. However, in the present study, there was not much difference in the proportion of females getting admitted for gastrointestinal surgeries compared to men over the study period from 1996 to 2018 (36% in 1996-1998 vs. 38% in 2016-2018).

However, when biologically compared most studies conclude that females often fare much better than males with regards to all sorts of outcomes after gastrointestinal surgery or major trauma. These outcomes include mortality, duration of hospital stay, fewer emergency procedures and better outcome even after emergency operations. This advantage of the female gender has been attributed to the effects of oestrogen on the immune system [33]. In various previous studies it has been documented that males have poorer outcome compared to females after trauma or in the presence of sepsis [34] [35] [36] [37]. Even in this retrospective study, it was found that females had an overall lower in-hospital mortality rate compared to males ($p < 0.001$). Females also had a lesser mean duration of hospital stay compared to men (10.3 vs. 11.8 days; $p < 0.001$).

Oestrogen can modulate the immune system through its receptors on various immune cells including T- cells, monocytes and macrophages [38] [39] [40]. It causes changes in cytokine production, cell activation and proliferation. The gonadal hormones oestrogen and testosterone influence immune and cardiac function following trauma, haemorrhage and shock. It has been observed, in a study in mice, that females had a better immune response compared to their male and ovariectomized female counterparts following trauma and hemorrhage [41] [42]. This suggested that oestrogen might have a protective role in this type of injury [43]. There were also other studies which observed these differences in humans and mice after trauma-haemorrhage, with males having an increased incidence of MODS (Multiple Organ Dysfunction Syndrome) and sepsis [44]. In

another clinical study patients with multiple injuries were evaluated and it was observed that females in the study had significantly lower levels of IL-6 and IL-8 in serum at an early stage and lower levels of IL-10 at a later stage after injury compared to males. Consequently, females maintained a better functional immune response following sepsis and had better survival rate than males after sepsis [45] [46].

Studies on gender difference in outcomes after gastrointestinal studies from the west also show a significantly improved mortality in women after different surgery types like gastric, small intestinal, large intestine, hepatic and pancreatic [9] [47]. But in our study males had significantly better survival rates after liver and pancreatic surgeries ($p < 0.001$) and, though not significant, had better a survival rate after splenic surgery. In all the other types of surgeries females had better survival rates but this was not statistically significant. This is probably because of the cultural constraints with females presenting later in the disease course in developing communities compared to females of the developed communities.

One study from Glasgow, Scotland also found that outcome after emergency surgeries was found to be dependent on gender with females having better outcomes. We found in that females had significantly lesser proportion of emergency surgeries compared to males ($p < 0.001$), but mortality after emergency surgeries though better in females was not significant ($p = 0.056$).

5. Conclusions

In conclusion, we found that though females fared better than males in outcomes after gastrointestinal surgeries, the difference was not significant as has been observed in the developed countries possibly because of our cultural gender differences in hospital seeking behavior. This higher mortality rate might probably also be because of higher number of males getting admitted in tertiary hospitals for treatment compared to females. Though the proportion of admitted patients who received treatment fluctuated over time, the proportion of women always remained lower than the proportion of men.

The effects of oestrogen on outcomes following injury are a growing area of research and further studies are required to firmly establish this relationship. But in developing countries like India, it is necessary to create policy approaches directed towards better communication and medical awareness to enhance the medical care we provide for females.

Limitations

This is a single, tertiary centre study and so probably the results cannot be applied to the Indian population. The differences in incidence of pre-operative or post-operative complications and hospital charges incurred between males and females were not evaluated which might be other interesting areas for future investigation. Also, the gender differences in outcomes among different age groups

were not evaluated which could have highlighted the influence of age on hospital seeking behavior among males and females.

Ethical Approval

The article has been submitted and the certificate will be uploaded in due time.

Conflicts of Interest

The authors of this study certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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