Colorectal cancer at Tribhuvan University Teaching Hospital

- A retrospective study 2064-2067

Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Master thesis in Medicine

Author: Lotten Lord

Supervisor: Göran Kurlberg, PhD, Yogendra Singh, PhD
Department of Surgery, Sweden and Nepal



UNIVERSITY OF GOTHENBURG

Programme in Medicine Gothenburg, Sweden 2013

Table of Contents

Abstract	3
Introduction	5
Nepal	5
Colorectal cancer epidemiology	6
Factors associated with CRC	8
Symptoms and signs	8
Treatment	9
Prognosis	9
Aim	10
Material and Methods	10
Sample	10
Data collection	11
Statistical analysis	11
Ethics	12
Results	13
Age and sex	13
Ethnicity	15
Symptoms and signs, surgical method and localization	15
Staging	17
Discussion	18
Limitations	21
Conclusions	21
Populärvetenskaplig sammanfattning	23
Acknowledgements	25
References	26

Abstract

Master Theses Project, Programme in Medicine

Colorectal cancer at TUTH – a retrospective study 2064-2067

Lotten Lord, 2013

Department of Surgery, Institute of Clinical Sciences at Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Background

Colorectal cancer (CRC) is one of the most common types of cancer worldwide. In Asia the incidence of CRC is increasing and is now the third most common malignant disease. There is limited research on CRC in Nepal. It is of great importance to investigate this issue further.

Aim

The aims were to describe demographic data regarding patients treated for CRC at Tribhuvan University Teaching Hospital (TUTH) in Kathmandu, Nepal, during a three year period (2007-2010), symptoms and signs during first consultation, localisation and staging, and type of surgical procedure. Furthermore to investigate differences between age, sex, ethnicity with regard to incidence of malignant tumors, and its staging.

Methods

Medical records of patients (n = 83) with primary CRC at TUTH were reviewed during a three years period.

Results

Colon was most frequent site (58 %) of malignant tumor, colon to rectal ratio being 1.4:1. Mean age in the total group was 53.6 ± 15.6 years. Number of patients under 40 years of age

was 13 (16.0 %). There were 53 men and 30 women, the ratio being 1.8: 1. About 50 % of the

patients had Stage III-IV. No significant differences between age, sex, ethnicity with regard to

occurrence of CRC, and staging of tumor were found.

Conclusions

This study confirms an increasing number of CRC at TUTH compared to a study made in

2002. Though in contrast to other studies a lower occurrence of CRC among patients under 40

years of age (16 %) was found. Although earlier assumed genetic heritage in the two

bordering countries, China having an incidence rate 3.8 times higher than India, this

difference was absent at TUTH, indicating environmental factors to contribute more than

genetics. A remarkable high proportion of advanced stage of presentation account for poor

prognosis. The number of patients is limited and therefor further studies with larger materials

are required.

Key words: Colorectal cancer, Ethnicity, Localization, Nepal, Staging, Symptom and Sign

4

Introduction

Nepal

Preliminary results of the National Population Census 2011 show that the population of Nepal had reached 26.6 million, which is an increase of the population at the rate of 1.4 % per annum. The sex ratio is estimated to 94.41 (male per hundred female). The preliminary results reveal that the population of male is 12.9 and female population is 13.6 million. In the last 15 years age structure has changed in Nepal, the proportion of children, 15 years and younger has decreased to 36.7 % while those 15-59 years has increased to 54.2 %. The group 60 years and above makes up only 9.1 %. Among the urban areas the district of the capital Kathmandu has the highest number of cohabitants with 1.7 million people.³ The population can be divided into different groups based on different parameters, such as language, geography, cast, religion and ethnicity. There are several ethnic groups in the Nepali population.² Due to Nepal's location between India and China, they can be divided into two main groups: the Indo-Aryan group, which account for 60 % and the Tibeto-Mongolian group with 40 %. Although, urbanization has mixed the society somewhat, different casts still live in separate communities and according to different traditions. Marriage often occurs within the same cast and almost exclusively within the same ethnicity. These homogenous ethnical groups offer an opportunity to study the genetical impact on these societies.

Nepal is among one of the poorest countries in the world, with a total BNP of 15700 \$ in 2010. Although living standards have improved in Nepal during the last decades there are still large differences between regions, with major gaps between rich and poor, as well as large varieties in educational level.² Agriculture accounts for 38 % of the economy, and though its importance has decreased since the 1970's it remains the second most common source of income. The industry and aid from other countries are also important sources of income.⁴ Educational attainment is directly related to status of an individual. The literacy rate

has increased during the last 15 years, but it is still only 61 % of the population of six years and above. In urban areas the literacy rate is substantly higher (77 %) compared to rural areas (57 %). There are also differences between men (72 %) and women (51 %).² The expected life time in Nepal is 69 years for women and 68 years for men.⁴

In most Asian countries, national healthcare systems and health insurance cover only a minority of people. In many rural areas and communities of low socio-economic status, people have limited access to healthcare facilities.³ The average consumption of health care is 20 \$ per year.⁴ Most people (63 %) attend private health institutions, the remaining visit government institutions such as hospitals and pharmacies. For both private and government institutions the consultations are more expensive in urban areas compared to rural.² The total number of hospital beds in Nepal are 6944 (2007/2008)¹, 444 of these being at Tribhuvan University Teaching Hospital (TUTH)⁵, which is a government hospital in Kathmandu, offering some private services.

Colorectal cancer epidemiology

Colorectal cancer (CRC) is one of the most common types of cancer worldwide. CRC is the third most common type of cancer in males and the second in females with the highest rates in Australia, New Zealand, and Western Europe. CRC accounts for 8 % of all cancer deaths and is the fourth most common cause of death from cancer. In Central and Eastern Europe CRC accounts for the highest mortality in both males and females. In Asia the incidence of CRC is increasing and research shows that this type of tumor is the third most common malignant disease in both men and women. In Eastern Asia, countries such as China, Japan, South Korea and Singapore show a two- to four-fold increase in incidence in recent decades. The Chinese National Cancer Database of 2003 shows that CRC was one of the cancers with the most rapidly increasing incidence. While other cancers decreased, CRC increased over two decades in a province with 9 million inhabitants in China. The incidence of CRC is significantly

higher among the Chinese compared to other ethnic groups in Asia. A low incidence of CRC has been shown in India to but an increase in the incidence of colon cancer has been reported for both men and women, but the rates of rectal cancer are steady. The world-age-standardized incidence rate in India is 4.3 and in China 16.3 (3.8 times higher). Pourhoseingholi concludes that there is little support in health authorities for CRC screening in Asia. Furthermore the public awareness of CRC is very low.

Nepal does not report on cancer incidence to WHO, and so far calculations for CRC incidence in Nepal have only been estimated from data of the bordering countries India and China. The genetic background of Nepal's population and the more homogeneous environment, make Kathmandu and its surroundings an interesting location for studies on etiology of cancer. Only one larger study regarding cancer has so far been made in Nepal covering patients from seven major hospitals in the country, colon represented 1.6 % and rectal cancer 2.4 % of the total cancer causes (ratio 1:1,5). ¹³ In a further detailed report on 245 of the rectal cancer cases from the multi-hospital statistics, the colorectal cancer patients represented, 1.85 % of the total number cancers, men to women ratio 1,1: 1. The group was more commonly originating from lower to middle economics, age being generally younger (median age 46.5), with 26.55 % of the patients diagnosed below 34 years of age and totally 45.11 % diagnosed below 44 years of age. This deviates from the international scenario. 14 Corresponding figures from the USA, the average age of onset is 70, and the percentage of cases diagnosed according to different ages is 1.2 % below 34 and totally 5.0 % below 44 vears of age. 15 Significantly young age at debut of CRC was also reported in a retrospective study, covering a 5-year period, from Tribhuvan University Teaching Hospital (TUTH) published in 2002. In this study 28.6 % of the CRC patients were younger than 40 years of age, with a predominance for female sex. In this young group it was significantly more common with left sided CRC and more aggressive tumors. 16

Factors associated with CRC

Migrants to the United States from Asia have long been recognized as an informative population to study for the purpose of surveying to what degree genetics plays a role in developing different cancer types, as well as for identifying possible environmental factors that may be responsible for the worldwide variations in incidence rates.¹⁷ Regarding CRC, although incidence rates for rectal and colon cancer are both low in studies from India there is a rise in incidence, above all among migrants and urban Indians compared to those still living in rural areas.¹⁸ This indicates changing environmental factors to be a cause of resent decades rise in incidence. Japanese immigrant studies show the same pattern with a time-dependent successive increase of incidence among Japanese' whom had migrated to the United States.¹⁹

Studies about which environmental factors are associated with an increased or decreased risk to develop CRC show different results. However, some factors are recurrent. Possibly associated with a decreased risk are for example fresh fish^{20,21}, soluble dietary fibers²² and physical activity.^{22,23} On the contrary red meat¹⁸, dried fish¹⁹, obesity, high alcohol intake and long-time smoking^{22,23} might increase the risk.

Symptoms and signs

Reasons for the patients choice to consult a doctor may vary. In colorectal cancer around 20% present with an acute onset of abdominal pain caused by bowel obstruction and / or perforation. More often the symptoms are anemia and changes in bowel habit. For right sided tumors also melena can occur. For rectal cancer it is not uncommon that fresh blood and / or mucus in feces as well as changes in bowel habit is the cause for seeking consultation. In later stages symptoms of CRC can be significant weight loss, loss of appetite, fatigue and obstruction, or a palpable lump in abdomen or rectum. ^{23,24}

Surgical treatment

The treatment for all CRC is surgery.²⁴ For tumors seated in right colon or the right half part of the transverse colon the surgical method is right hemicolectomy. Tumors seated in the distal transverse or in the descending colon are removed using left hemicolectomy with anastomosis. Cancers in sigmoideum are removed using sigmoidectomy with anastomosis.

Patients presenting with rectal cancer undergoes treatment with radiation before surgery. Depending on location different methods are used for tumor removal. Same for all is that Total Mesorectal Excision (TME)-surgery is used. When tumors are seated in superior part of rectum high anterior resection with a partial TME is performed, while in the mid rectum usually low anterior resection (LAR) is used. If the inferior part of rectum is involved abdominoperineal rectal resection (APR) with sigmoideostomy is the method of choice. Adjuvant therapy with 5-Fluorouaracil is offered to all patients with spread to regional lymph nodes.

Prognosis

The prognosis is dependent on the stage of cancer when detected. As a measure of severity the TNM classification is used (Table 1).²⁴ T describes the size and spread of the primary tumor, N the distribution to regional lymph nodes and M if there are metastasis.

Table 1. TNM-	classification in co	olorectal cancer.	
TNM			
Stage 0	ТО	N0	M0
Stage I	T1	N0	M0
	T2	N0	M0
Stage II	T3	N0	M0
	T4	N0	M0
Stage III	Any T	N1	M0
	Any T	N2	M0
Stage IV	Any T	Any N	M1

(Source: Lindmark G.: Kolon och rektum. In Kirurgi (2nd ed). Eds. Jeppson B., Naredi P., Peterson H-I., Risberg B. Lund: Studentlitteratur, 2008, p 298.)

In a western country, such as Sweden, the 5-years survival rate for men are 57.4 % in colon cancer and 57.3 % in rectal cancer. For women the numbers are 61.7 % in colon – and 60.4 % in rectal cancer. The 10-years survival rate for men is 51.4 % in colon cancer and 46.8 % in rectal cancer. Corresponding numbers for women are 56.8 % and 51.8 %.²⁵

The incidence of colorectal cancer has increased in several countries in Asia. However, there is limited research on colorectal cancer in Nepal. There are also differences between the incidence in China and India. The ethnic variety of Nepal's population makes it interesting to study possible differences among the ethnic groups.

Aim

The aims of this study were to describe demographic data regarding patients treated for CRC at Tribhuvan University Teaching Hospital (TUTH) in Kathmandu, Nepal, during a three year period (2007-2010), symptoms and signs during first consultation, localization and staging of primary colorectal tumor, and what type of surgical procedure that had been performed. Further more to investigate differences between age, sex, ethnicity with regard to incidence of malignant tumors, and its staging.

Material and Methods

Sample

Records from patients at TUTH during the period of Nepali year 2064 until 2067 (2007-2010) were included in the study. The inclusion criteria was that each patient had been diagnosed with CRC. First step meant going through surgery register where all surgery patients were listed with a number, diagnosis and surgery method. The second step was to locate each patient's medical record, which were handwritten in English. Name and id-no for a total of 97

patients, who had been given the diagnosis colon and/or rectal cancer were collected. Out of those 97 patients 83 medical records could be found.

Data collection

Data concerning age, sex, ethnicity (Indo-Aryan, Tibeto-Mongolian or other), primary tumor localization (colon: Ascending, transverse, descending, sigmoid, rectum: High, middle, low), as well as symptoms and signs when first time consulting a doctor was searched for. Also, what type and number of procedures each patient had so far undergone (right or left hemicolectomy, sigmoidectomy, total colectomy, low anterior resection, Hartmann's procedure, abdominoperineal rectal resection, non-curative operation, non-operative treatment), and staging of tumor (TNM) was collected. Patients leaving against medical advice were registered as LAMA. For site of tumor localization, colon was further separated into *left* or *right* (proximal or distal to left flexure), and rectum into *low* or *mid-high* (≤ 5cm or > 5cm from anal verge). The first ten medical records were read together with my colleague, to check that we interpreted the content of the records alike and used the same way of cataloging the data.

Statistical analysis

Analysis of clinical data with reference to number, percentage, mean, median and range was performed using the computer program IBM® *SPSS Statistics 19*. Mann-Whitney *U*-test was used to test differences between sex and age and between occurrence of CRC (colon and rectum) at TUTH and age. Age was divided into two groups, < 40 years $/ \ge 40$ years, to enable comparison with the earlier study at TUTH. Chi-square tests were used for testing differences between nominal variables regarding age groups (< 40 years $/ \ge 40$ years), sex (male / female), ethnicity (Indo-Aryan / Tibeto-Mongolian) and occurrence of CRC (colon,

colorectal and rectal) at TUTH and staging of tumor. When the numbers were five or less in one or more cells Fisher's Exact test was performed. Statistical significance was set at $p \le 0.05$.

Ethics

Permission to review the records was given by professor Yogendra Singh, TUTH. The study was conducted according to the Helsinki declaration.²⁶ All records were given a number and the data was treated anonymously. Ethics approval was not required since there was no ethical committee established at the hospital.

Results

A total of 97 patients were identified as being diagnosed with, or treated for, colorectal cancer at TUTH, during the time 06.2007 to 06.2010. Mean number of patients per year 2007-2010 was 32.3 (total number 97 under a three-year period). Out of those 97, 14 were excluded, because of inability to locate the record files concerned. For the remaining patients, demographic data (age, sex, ethnicity), symptoms and signs, localization of colorectal tumor in GI-tract, type of procedure used for removing cancer, and staging are presented.

Age and sex

The mean age in the total group of patients was 53.6 ± 15.6 years (md 55, range 18-87). For the 30 women the mean age was 54.7 ± 14.9 (md 55.5, range 18-85) and for the 53 men mean age was 53.0 ± 16.0 (md 54.0, range 21-87). There was no significant difference between males and females regarding age (Z = 0.484, p = 0.628).

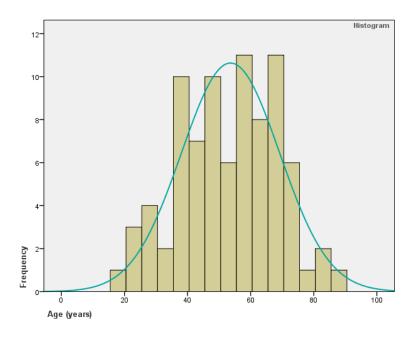
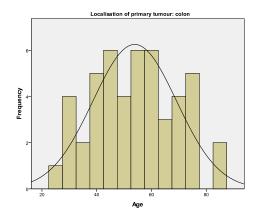


Figure 1. Age at diagnosis of CRC, distribution regarding colon and rectal tumors (n = 83).

The distribution of at which age a patient first had been diagnosed with tumor in colon and / or rectum for the whole group appeared with a wide range (Figure 1). The youngest patient

being diagnosed with rectum cancer was at the age of 18 and the oldest one with colon cancer at the age of 87 (Figures 2 and 3).

Comparisons between the two tumor locations in relation to age at diagnosis showed no significant differences (Z = 0.250, p = 0.882). The numbers under 40 years old was 13 (16.0 %) for all CRCs.



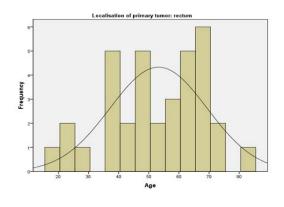


Figure 2. Age at diagnosis, distribution regarding colon tumor (n = 48).

Figure 3. Age at diagnosis, distribution regarding rectum tumor (n = 35).

The overall men to women ratio was 1.8 to 1 (Table 2). Though men represented 2/3rds of colon cancers compared to only 3/5ths of the patients with rectal cancer, there were no significant differences between sexs regarding localization ($x^2 = 0.390$, p = 0.532).

Table 2. Occu	ırrence	of colo	ectal cancer.		
	(Colon	Rectal		Overall
	C	ancer	cancer		
	n	%	n	%	n %
N	48		35		83
% of cases		58	4	2	100
Sex					
Female	16	53	14 4	7	30 36
Male	32	60	21 4	0	53 64
					TUTH, Kathmandu, Nepal, 06/2007 – 06/2010.

The number of males under 40 years old was 9 (19 %) and the equivalent for females was 4 (13.2 %) for all cancers. More of the females under 40 years old had colon cancer, 3 (75 %), than rectal cancer, 1 (25 %). The localization of primary tumor in males was in colon, 5 (56 %) and in rectum, 4 (44 %). No significant differences were found between sexes under 40 years regarding localization ($x^2 = 0.090$, p = 1.000).

Ethnicity

In four records no data on ethnicity was found. The records for the remaining 79 patients treated for CRC at TUTH showed that 63 % were Indo-Aryan and 37 % Tibeto-Mongolian. The occurrence of colorectal cancer related to ethnicity is shown in Table 3. No significant difference was found between the two ethnical groups and localization of tumor ($x^2 = 0.018$, p = 1.000).

Table 3. Occurrence rega	arding to ethnicit	ty (n = 7	9, missing = 4).	
	Indo-	-Aryan	Tibeto	-Mongolian
	n	%	n	%
Colon cancer	28	56	16	55
Rectal cancer	22	44	13	45
			TUTH, Kathmandu, Ne	pal, 06/2007 – 06/2010

Symptoms and signs, surgical method and localization

The patients' various symptoms and signs for colon and rectal cancer found in the records are presented in numbers and percentages (Table 4). Pain in abdomen (65 %), anemia (52 %), change in bowel habit (48 %), and blood in faeces or melena (48 %) were the most frequent symptoms and signs for patients with colon cancer. Blood in faeces or melena (74 %), change in bowel habit (66 %), pain in abdomen/rectum (63 %), and palpable lump p/r (63 %) were most common for patients with rectal cancer.

Table 4. Symptoms and signs					
Colon cancer	n	%	Rectal cancer	n	%
	48			35	
1. Pain, abdomen	31	65	1. Blood in faeces or melena	26	74
2. Anemia	25	52	2. Change in bowel habit	23	66
3. Change in bowel habit	23	48	3. Pain, abdomen/rectum	22	63
4. Blood in faeces or melena	23	48	4. Palpable lump, P/R	22	63
5. Weight loss (significant) ¹	20	42	5. Anemia	19	54
6. Palpable lump	19	40	6. Weight loss (significant) ¹	18	51
7. Loss of appetite	18	38	7. Discomfort, rectum	16	46
8. Fatigue	11	23	8. Loss of appetite	13	37
9. Obstruction	7	15	9. Fatigue	6	17
			10. Obstruction	6	17
¹ Significant level 10 % of body weight lost in	3 months or	5 % in 1 month.	TUTH, Kathma	ndu, Nepal,	06/2007 – 06/2010.

When looking at what kind of procedure had been performed on first occasion of surgery, the patients were divided into groups depending on tumor localization. For twelve patients, surgery records or information about treatment could not be found. Out of the 71 remaining cases, 51 hade undergone curative surgery, 13 patients had had palliative surgery and six had been given other palliative treatment (Table 5). One patient left against medical advice.

	Colon, left		Colon, right		Rectum, mid- high		Rectum, low		Total	
	n	%	n	%	n	w %	n	%	n	%
Right hemicolectomy			16	59					16	23
-extended	3	20	2	7					5	7
Left hemicolectomy	5	33							5	7
Sigmoidectomy	3	20							3	4
Total colectomy	1	7	1	4					2	3
Low anterior resection	2	13			7	47			9	11
Abdominoperineal rectal resection	on				1	7	10	71	.11	16
Palliative surgery			4	15	5	33	4	29	13	18
Palliative treatment	1	7	3	11	2	13			6	9
LAMA			1	4					1	2
									7	'1
Total	15	100	27	100	15	100	14	100	10	00
Missing			8		2		1		12	

Staging

Classification (staging) was documented in 64 records. Almost 50 % of the patients with colon cancer had Stage III-IV and for rectal cancer the percentage was even higher (Table 6). There were no significant differences between the type of cancer ($x^2 = 3.678$, p = 0.298).

Table 6. TNM-class	sification in colorect	al canc	er.		
Stage	Colon ca	ncer	Rectal ca		
Stage	n	%	n	%	
Stage I	5	14	6	21	
Stage II	14	39	7	25	
Stage III	7	19	10	36	
Stage IV	10	28	5	18	
			TUTH, Kathmandu, I	Nepal, 06/200	07 – 06/2010.

TNM-classification in CRC regarding sex, age groups (< 40 years and \geq 40 years), and ethnicity is shown in Table 7. More males (56 %) had Stage III-IV. The trend was similar for patients 40 years and above and for Indo-Aryans. However, significant differences were not found between the sexes ($x^2 = 3.557$, p = 0.313), the groups of patients under 40 years and 40 years and above ($x^2 = 0.493$, p = 0.920), and ethnicity ($x^2 = 1.960$, p = 0.581).

Stage	Mal	es	Fem	nales	< 40) years	<u>></u> 4	0 years	Indo	o-Aryan	Tibe	to-Mongolian
	n	%	n	%	n	%	n	%	n	%	n	%
Stage I	5	13	6	24	2	20	9	17	6	15	5	25
Stage II	12	31	9	36	4	40	17	31	13	32	7	35
Stage III	10	25	7	28	2	20	15	28	10	24	5	25
Stage IV	12	31	2	12	2	20	13	24	12	29	3	15

TUTH, Kathmandu, Nepal, 06/2007 – 06/2010.

Discussion

In this retrospective study where 83 records of patients with CRC at TUTH were examined from a three-year period, the occurrence of colon cancer was 58 % and 42 % for rectal cancer. No statistical significant differences between age, sex and ethnicity with regard to occurrence of cancer tumors and staging of tumor were found.

Mean number of patients per year 2007-2010 were 32.3 (total number 97 under a three-year period) compared to 18.2 1996-2001 (91 patients under a five-year period), indicating that the number of patients may be increasing. The overall men to women ratio for CRC was 1,8:1, the corresponding distribution worldwide is 1,4:1, and for China 1,32:1 and India 1,25:1. However, it could not be assumed that men being more diseased with CRC than women is a representative result throughout the whole of Nepal, since our material consist of a rather limited number of patients in a single hospital. Though results from other Nepalese hospitals also show a high men to women ratio. 12,28

The patients with CRC being below 40 years of age accounted for 16 %. In the previous study from the same hospital in Nepal the number was much higher, 29 %¹⁶, and in a more recent study 28 %.²⁹ Other studies, also indicating a rise in colorectal cancer among young adults, do not agree with the present study. Furthermore, these results revealed a higher occurrence for males (19 %) versus females (13 %), in the recent study by Kansakar and Singh the male female ratio changed from 2:3 (1999-2003) to 4:3 (2004-2008).²⁹ The contrasting results regarding patients below 40 years makes this important to study further.

Over 50 % of the patients had Stage III-IV cancers. The number of younger patients below 40 years who had Stage III-IV was 4 (40 %), not significant between the age groups (<40 years vs. \ge 40 years) in this study. Studies from Nepal and other countries found that younger adults often presented with more advanced CRC, stage III-IV. $^{16,29-31}$ The 2 years survival rate was found to be lower for younger patients than for older patients. 16 Also, 94 %

of young patients who died did that within 20 months of operation, while for those who survived the prognosis was improved.³¹ There are several possible explanations to why younger people present with later-stage tumors. Delay in diagnosis may depend on delayed presentation, bad access to health care or misdiagnosis.²⁹ Other explanations are environmental or genetic influences. There are several known risk factors for CRC which also are confirmed in a recent study of younger patients in Italy and Switzerland.³² Family history of CRC was the strongest predictor in the younger patients compared to middle aged and elderly patients. Patients delay may be one cause leading to diagnosis at a later stage contributing to lessened prospects for cure. At TUTH 72 % (51/71 patients) of the surgical procedures were curative. This result might be difficult to compare with other hospitals not equal in standards and organization. Increased awareness about cancerous diseases could help limit patients delay and contribute to better prognosis.

Localization of the colorectal tumors had a somewhat predominance for colon cancer, with a ratio of 1,4:1. These results agree with colon cancer being more common than rectal cancer in USA¹⁵ and in Scandinavia.³³ This result on distribution of CRC though, was not consistent to the results from the larger investigation directed by BP Koirala Memorial Cancer Hospital in Nepal¹³, in which rectal cancer was more common than colon cancer. Also in India incidence rate for rectal cancer exceeds colon cancer. However, in Mumbai a significant rise of incidence in colon cancer has been reported, whereas rectal cancer remains at the same level. The incidence of CRC in urban areas is approximately the double than in rural areas.¹¹

No significant differences was found regarding possible genetic impact. This by itself is a remarkable result especially when keeping in mind the much larger incidence of CRC in China compared to India.⁷ With this background one could expect an overweight of cases among the Tibeto-Mongolian group versus the Indo-Aryan, which was not the case. This might implicate that the genetic factor plays a minor role in developing CRC and that

environmental factors play a more central part. This can be compared with studies from India showing CRC to be more common among urban Indians¹⁸, as well as studies made on Japanese migrants.¹⁹ Differences in environmental factors can be a more western life style with among other changed dietary habits, higher alcohol intake and tobacco smoking, and less physical activity. Curcumin in turmeric, a common spice in Indian cooking, has on the other hand been shown to have a preventative effect on colon cancer genesis.^{34,35} The use of turmeric and a high intake of starch within Indian food may attribute to the low level of incidence of colon cancer in India.

TUTH has a large catchment area, therein Kathmandu. Since there were no specific limits in patient area uptake, there could be no valid number of the population exposed to risk of CRC to relate our collected data with, this limiting the results of the study to be a descriptive epidemiology study of a number of cases, and no statistics on occurrence could be calculated.

A lot of the patients had several symptoms and signs. The most frequent symptom in patients with colon cancer was abdominal pain (65 %), followed by anemia (52 %), change in bowel habit (48 %), and blood in faeces/melena. Corresponding figures in patients with rectal cancer were blood in faeces/melena (74 %), changes in bowel habit (66 %), pain in abdomen and rectum (63 %), and palpable lump in rectum (63 %). Those symptoms were also found to be the most common in another study and a median of three symptoms was found in all CRC patients. Rectal bleeding as an initial symptom was found to correlate with less advanced staging and reduced mortality, whereas mild anemia correlated with more advanced staging and worse mortality. Tearly CRC may have significant symptoms comparable to advanced CRC, to improve survival early detection is important. However, the symptoms are highly unspecific, various infectious diseases are frequent in Nepal, and symptoms and signs from a CRC can in some cases be interpreted as those of a non-cancerous origin. Broad-spectrum

antibiotics can be bought from pharmacies without prescription before seeking medical care and pass through proper examination, causing patient's delay. In addition, according to different traditions, some minor ethnicity there is still custom to seek help from a holy person, instead or before seeking medical care. Patients delay and poor knowledge about cancerous diseases, are therefore important factors to acknowledge.

Limitations

The patient medical records at TUTH are archived for three years only, because of narrowed storing space, thereby limiting the time period and number of patients to study. Also, 14 of the 97 records were never found although repeated attempts to locate them were undertaken. Because of no data available for the 14 missing patients there was not possible to conduct a drop-out analysis. There were also internal drop out for different variables because of pages being lost from some of the records and in some cases it was difficult to interpret the handwritten text. The handwritten filing system may have caused possible misinterpretation. The limited number of patients in just one hospital make the results difficult to generalize.

Conclusions

This study confirms an increasing number of CRC at TUTH. In contrast to other studies there was a lower occurrence of CRC among patients under 40 years of age (16 %). The overall male to female ratio was 1,8:1, following the worldwide trend. Although earlier assumed genetic heritage in the two bordering countries, China having an incidence rate 3.8 times higher than India, this difference was absent among the population diagnosed with CRC at TUTH. This may indicate that environmental factors contribute more than genetics. The most common symptom among patients with colon cancer was pain in abdomen, and for patients with rectal cancer blood in faeces or melena. The remarkable high proportion of advanced stage of presentation account for poor prognosis. Urbanization and change of living-habits

may have had an affect on the increasing level of CRC among the population in Kathmandu. To further investigate this is necessary. Another focus should be on genetic impact and environmental risk factors. The limited number of patients require further studies with larger materials taking account more regions in Nepal. Introducing systematic nationwide statistics on cancer in the future would be valuable for studies on cancer epidemiology in Nepal.

Populärvetenskaplig sammanfattning

Denna studie från 2013 (2007-2010) visar att tjock- och ändtarmscancer har ökat på ett sjukhus i Kathmandu, Nepal, sedan förra studien 2002 (1996-2001). Däremot är andelen unga vuxna, patienter under 40 år, något lägre än tidigare.

Befolkningen i Nepal kan i huvudsak delas in i Indo-arier, härstammande från Indien, och Tibeto-mongolier, från Tibet och Kina. I Kina är denna typ av cancer 3,8 gånger vanligare än i Indien, därför har man antagit att det finns ett genetiskt inslag som kan förklara uppkomsten av cancer. I den här studien fanns dock ingen skillnad i incidens av cancer mellan de två etniska grupperna vilket skulle kunna peka på att miljöfaktorer spelar en större roll när det gäller uppkomst av tjock- och ändtarmscancer. En anmärkningsvärd hög andel av patienterna hade långt framskriden cancer, vilket ofta talar för en dålig prognos med kortare överlevnad. Dålig kännedom om sjukdomen och en hög förekomst av tarminfektioner i landet, med liknande symtom, kan göra att patienterna söker sjukvård sent.

Tjock- och ändtarmscancer är en av de vanligaste cancertyperna i världen. I Asien har sjukdomen tidigare varit relativt ovanlig, men på senare år har man på vissa håll sett en betydande ökning. Det är nu den tredje mest förekommande cancerformen. I Nepal har forskning inom området varit mycket begränsad och det är viktigt att studera vidare för att få mer kunskap.

Studien är genomförd i Kathmandu, Nepal, på sjukhuset Tribhuvan University Teaching Hospital (TUTH). I arbetet granskades handskrivna pappersjournaler till patienter som under de tre senaste åren fått diagnosen tjock- och ändtarmscancer på TUTH. Av totalt 97 patienter kunde 83 journaler hittas. Granskningen omfattade ålder, kön, etnicitet, tumörlokalisation, symtom och tecken vid diagnostik, behandling samt cancerstadium.

En mer västerländsk livsstil på olika håll i Asien verkar bidra till utveckling av tjockoch ändtarmscancer. I större städer och bland migranter är cancerformen vanligare. Kända riskfaktorer är till exempel olika matvanor, högt intag av alkohol samt rökning. Några skyddande faktorer är fysisk aktivitet, stärkelserik föda och curcumin som finns i gurkmeja.

Många länder har ett dataregister innefattande olika cancerformer som täcker hela landet. Ett sådant system saknas fortfarande i Nepal, men skulle vara betydelsefullt att införa för en kontinuerlig kartläggning. Fler studier som omfattar graden av miljö- versus genetiska faktorer behövs också.

Acknowledgements

I want to thank my supervisors associate professor Göran Kurlberg and professor Yogendra Singh for excellent guidance. I would also like to thank MD Yogendra Shakya for hospitality and generosity.

References

- 1. http://census.gov.np/ (accessed 2012-11-19)
- 2. Nepal living standards survey. Statistical report, nr 1. Central Bureau of Statistics, National Planning Commission Secretariat, Government of Nepal, Nepal: 2011.
- 3. National Population Report, Government of Nepal, Ministry of Population and Health, Population Division, Ramshahpath, Kathmandu, Nepal: 2011.
- 4. Landguiden, Utrikespolitiska institutet.

 http://www.landguiden.se/Lander/Asien/Nepal (accessed 2012-11-19)
- 5. Tribhuvan University Teaching Hospital. www.teachinghospital.org.np (accessed 2012-12-14)
- 6. Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010,127:2893–2917.
- 7. Sung JJ, Lau JY, Goh KL, Leung WK. Asia Pacific Working Group on Colorectal Cancer. Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol 2005,6:871-876.
- 8. Lu JB, Sun XB, Dai DX, Zhu SK, Chang QL, Liu SZ, Duan WJ. Epidemiology of gastroenterologic cancer in Henan Province, China. World J Gastroenterol 2003,9:2400-2403.
- 9. Lee HP, Lee J, Shanmugaratnam K. Trends and ethnic variation in incidence and mortality from cancers of the colon and rectum in Singapore, 1968 to 1982. Ann Acad Med Singapore 1987,16:397-401.
- 10. Pathy S, Lambert R, Sauvaget C, Sankaranarayanan R. The incidence and survival rates of colorectal cancer in India remain low compared with rising rates in East Asia. Dis Colon Rectum 2012,55(8):900-906.
- 11. Mohandas KM, Desai DC. Epidemiology of digestive tract cancers in India. V. Large and small bowel. Indian J Gastroenterol 1999,18(3):118-21.

- 12. Pourhoseingholi MA. Increased burden of colorectal cancer in Asia. World J Gastrointest Oncol 2012,15(4):68-70.
- 13. Pradhanananga KK, Baral M, Shrestha BM. Multi-institutions hospital-based cancer incidence data for Nepal an initial report. Asian Pasific J Cancer Prev 2009,10:259-262.
- 14. Acharya B, Jha AK, Shretha S, Karn A, Bhandari RB, Poudel S, Sharma S, Neupane P. Rectal malignancies in B. P. Koirala Memorial Cancer Hospital: A 10-year experience. J Clin Oncol 2010,28 (suppl,abstr e14127).
- 15. National Cancer Institute, U.S National Institute of Health. http://seer.cancer.gov/statistics/ (accessed 2012-12-21)
- 16. Sing Y, Vaidya P, Hemandas AK, Singh KP, Khakurel M. Colorectal carcinoma in Nepalese young adults: presentation and outcome. Gan To Kagaku Ryoho 2002,29 suppl1:223-229.
- 17. Maskarinec G, Noh JJ. The effect of migration on cancer incidence among Japanese in Hawaii. Ethn Dis 2004,14(3):431-439.
- 18. Mohandas KM, Jagannath P. Epidemiology of digestive tract cancers in Indi. VI. Projected burden in the new millennium and the need for primary prevention. Indian J Gastroenterol 2000,19(2):74-78.
- 19. Sakamoto K, Machi J, Prygrocki M, et al. Comparison of characteristics and survival of colorectal cancer between Japanese-Americans in Hawaii and native Japanese in Japan. Dis Colon Rectum 2006,49(1):50-57.
- 20. Norat T, Bingham S, Ferrari P, et al. Meat, fish and colorectal colon risk: The European perspective investigation into cancer and nutrition. J Natl Cancer Inst 2005,97(12):906-916.
- 21. Ganesh B, Sanjay D, Rajesh D. A case-control study on diet an colorectal cancer from Mumbai, India. Cancer Epidemiol 2009,33:189-193.

- 22. Ahmed FE. Effect of diet, lifestyle and other environmental / chemoprevental factors on colorectal cancer development, and assessment of the risks. J Environ Sci Health, 2004,22(2):91-147.
- 23. Friedenreich CM, Neilson HK, Lynch BM. State of the epidemiological evidence on physical activity and cancer prevention. Europ J Cancer 2010,46:2593-2604.
- 24. Lindmark G. Kolon och rektum. In: Jeppson B, Naredi P, Peterson H-I, Risberg B, editors. Kirurgi (2nd edition). Lund: Studentlitteratur, 2008.
- 25. Bergman O, Hont G, Johansson E. Cancer i siffror 2009. Cancerfonden, Socialstyrelsen, artikelnummer 2009-129-127.
- 26. WMA Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. http://www.wma.net/en/30publications/10policies/b3/index.html (accessed 2012-12-21)
- 27. GLOBOCAN 2008 (IARC), Section of Cancer Information.

 http://globocan.iarc.fr/factsheets/cancers/colorectal.asp (accessed 2012-12-21)
- 28. Binu VS, Chandrashekhar TS, Subba SH, Jacob S, Kakria A, Gangadharan P, Menezes RG. Cancer Pattern in Western Nepal: A Hospital Based Retrospective Study. Asian Pacific J Cancer Prev 2007,8:183-186.
- 29. Kansakar P, Singh Y. Changing trends of colorectal carcinoma in Nepalese young adults. Asian Pasific J Cancer Prev 2012,13:3209-3212.
- 30. You N, Xing Y, Feig BW, Chang GJ, Cormier JN. Young-Onset Colorectal Cancer: Is It Time to Pay Attention? Arch Intern Med 2012,172(3):287-289.
- 31. Chan KK, Dassanayake B, Wickramarachchi RE, Kumarage SK, Samita S, Deen KI. Young patients with colorectal cancer have poor survival in the first twenty months after operation and predictable survival in the medium and longterm: Analysis of survival and prognostic markers. World J Surg Oncol 2010,15:8:82.

- 32. Rosato V, Bosetti C, Levi F, Polesel J, Zucchetto A, Negri E, La Vecchia C. Risk factors for young-onset colorectal cancer. Cancer Causes Control, 2012, DOI 10.1007/s10552-012-0119-3.
- 33. NORDCAN © 2009 Association of the Nordic Cancer Registries. http://wwwdep.iarc.fr/nordcan/SW/frame.asp (accessed 2012-12-21)
- 34. Johnson JJ, Mukhtar H. Curcumin for chemoprevention of colon cancer. Cancer Letters 2007,255:170-181.
- 35. Shishodia S, Chapurvedi MM, Aggarwal BB. Role of curcumin in cancer therapy. Curr Probl Cancer 2007,31:243-305.
- 36. Majundar SR, Fletcher RH, Evans AT. How does colorectal cancer present? Symptoms, duration, and clues to location. Am J Gastroenterolog 1999,94:3039-3045.
- 37. Stapley S, Peters TJ, Sharp D, Hamilton W. The mortality of colorectal cancer in relation to the initial symptom at presentation to primary care and to the duration of symptoms: a cohort study using medical records. British J Cancer 2006,95:1321-1325.
- 38. Smith D, Ballal M, Hodder B, Soin G, Selvachandran SN, Cade D. Symptomatic presentation of early colorectal cancer. Ann R Coll Surg Engl 2006,88:185-190.