BMJ Open Cancer in Lahore, Pakistan, 2010–2019: an incidence study

Farhana Badar ,¹ Shahid Mahmood²

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¹Cancer Registry and Clinical Data Management, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Punjab, Pakistan
²Cancer Registry and Clinical Data Management, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Correspondence to

Dr Farhana Badar;
farhana@skm.org.pk

ABSTRACT

Objectives To study the cancer incidence rates over 10 years (2010–2019), in Lahore, Pakistan.

Design An incidence study.

Setting The population-based Punjab Cancer Registry was established in 2005 in Lahore, which is the provincial metropolis of the province of Punjab (five rivers), and is located in the northeast region of Pakistan. The coordinating office of the Registry is located within Shaukat Khanum Memorial Cancer Hospital and Research Center. Both the active and passive forms of data collection are used.

Participants Residents of the district of Lahore diagnosed with cancer. The average annual population of Lahore was estimated at 11.1 million.

Outcome measures Cancer counts and incidence rates per 100 000 population, by age-group, sex and cancer site/type, over 10 years.

Results In Lahore, from 2010 to 2019, 58 394 incident cases were reported, with the majority seen in females (57.1%). Adults accounted for 92.2%, adolescents 2.2% and children 5.6% of the total cases. Per 100 000 population, the age-standardised incidence rate was 103.4 for females and 65.6 for males. Among females, the highest incidence rates were recorded for breast cancer (76.7) in adults, bone tumour (1.2) in adolescents and lymphoid leukaemia (1.6) in children, and among males, prostate cancer (10.7) in adults, bone tumour (2.2) in young adults and lymphoid leukaemia (2.4) in children. The age-specific incidence rates peaked in the 60–70 year group, reaching a high of 420 per 100 000 in women and 330 per 100 000 men.

Conclusions In Lahore, the incidence rates for cancers of the breast, prostate, lymphoid leukaemia and bone were among the highest documented. More cases were recorded in females than in males. The results reported could be used as a reference point for assessing the effectiveness of future interventions.

BACKGROUND

In 2020, Pakistan, categorised as a lower-middle-income country in South Asia, had a population of nearly 220 million with a Gross Domestic Product of US\$263 billion.¹ In such a heavily populated country, cancer registration should be a requirement for programme planning and evaluation to alleviate its morbidity and mortality. In reality, it is not so. Cancer surveillance is a challenging task in most developing countries of the world.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ As part of cancer surveillance, this is the first time that the age-standardised incidence rates have been presented for any region of Pakistan, over an extended 10-year period.
- ⇒ The age-specific incidence rates have been computed for cancers commonly diagnosed among females and males, in the district of Lahore, Pakistan.
- ⇒ Mortality statistics could not be generated because of the ongoing follow-up issues and the absence of a central death registry.

The latest version of Cancer Incidence in Five Continents, Volume XI (CI5 XI), published by the International Agency for Research on Cancer (IARC), shares information from 343 population-based cancer registries in 65 countries on cancers diagnosed from 2008 to 2012.² Of these 65 countries, 17 are in Asia. However, Pakistan is not listed in these countries. Population-based results from Pakistan were last included in CI5 Volumes VIII and IX, with the latter being released in 2007.³ The statistics were based on new cancer diagnoses within the geographically demarcated Karachi South district of the province of Sindh, representing a population of 1.7 million during 1998–2002.³ Karachi is a coastal town located in the southernmost part of the country, adjacent to the Arabian sea, at a distance of nearly 1200 km from Lahore.³ The Karachi Registry stopped functioning when Dr Yasmin Bhurgri, who had established the Registry, passed away in 2012. However, this Registry is now being revived.

A recent report on cancer incidence in the Karachi division for 2017–2019 has shown that the data were collected from eight centres of Karachi, which has a population of nearly 16 million, and that tobacco-related malignancies and breast cancer were the most common diagnoses.⁴ However, this report does not mention any problems related to the functioning of the Registry. Further, two reports representing the time periods 2010–2019 and 2010–2015 from a hospital-based cancer registry of Dow University in

Karachi indicate that the importance of cancer registration has been recognised, and this could pave the way for promoting population-based cancer registration in the region.^{5 6} Moreover, an institutional cancer registry has also been established by the Pakistan Atomic Energy Commission that collates data from 17 cancer hospitals of the Commission.⁷ Other than this, the Shaukat Khanum Cancer Registry, a hospital-based registry, has been in existence for more than 25 years and it collates and reports its data regularly.⁸ Additionally, efforts are being made to establish a National Cancer Registry in Pakistan though it is still in its initial stage.⁹

Cancer registration has been ongoing in Lahore for over a decade and the incidence rates have been reported in three different studies, with the last one covering a period of 6 years (2010–2015).^{10–12} Even though the incidence rates have been computed, both patient follow-up and collection of mortality data have been problematic throughout.^{10–12} Nevertheless, the study now being reported was conducted to determine the population-based cancer incidence rates in Lahore, by sex, age-group and cancer site/type, over 10 years. This is the first time that cancer statistics over a 10-year period are being reported for any region of Pakistan. It is hoped that the data provided will assist policymakers ascertain how healthcare delivery needs should be met most effectively through the allocation of existing and anticipated future resources.

METHODS

Study setting

Pakistan and the catchment area

There are five regions in Pakistan, and Punjab accounts for nearly 50% of the population of the country. Lahore is the capital and one of the 36 districts of Punjab.^{13 14} It is located in the northeast of the country, west of India.¹⁵ The total land area of the district is 1772 sq km, with the population density being 6300 per sq km.¹⁶ Nearly 95% of the residents of Lahore are Muslims, whereas only 5% constitute the minority.^{15 16}

Punjab Cancer Registry

History

In 2005, the Registry was established in Lahore, within a densely inhabited Punjab.¹⁷ The cancer incidence rates for the population of the district of Lahore have been reported in recent years but the mortality data could not be reported because of the continuing difficulty in establishing contact with nearly 50% of the patients, once they leave the treatment or diagnostic facilities they are attending.^{10–12} Second, the Registry does not have any data linkages with the National Database and Registration Authority, where a registration document is issued once the death of a person is notified to the Authority in the form of a death certificate from the graveyard and the Union Council.¹⁸ This has been problematic in estimating patient survival in the region.

Structure of the registry

The administrative centre of the Registry is the Cancer Registry and Clinical Data Management unit of Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&RC), Lahore, Pakistan. The focal persons involved in this project are an epidemiologist/biostatistician, medical coders and cancer registry officers, 10–13 in number. Over 40 members in 22 hospitals and laboratories in the private and government sectors report their cases to the central office (online supplemental appendix 1). This is through a mutual agreement between these centres. The representatives from these centres serve on the Governing Council of the Registry and assist in decision-making about the Registry. The Registry is sponsored by the Shaukat Khanum Memorial Trust, registered under the Societies Registration Act of Pakistan, and is a member of the International Association of Cancer Registries.

Data collection

The surveillance system uses both the active and passive forms of data collection from various hospitals and laboratories, thereby collecting detailed data on new cancer diagnoses among the residents of a geographically defined area of the district of Lahore, included in the catchment area of the Registry.¹⁷ Data sources include the medical records from inpatient admissions, outpatient/emergency assessment visits, hospital death certificates, pathology/operative reports, chemotherapy/radiotherapy logs, radiology/nuclear medicine reports and triage clinics. The information on the demographics and diagnostic findings is collected on a prescribed form with uniform data standards and definitions (online supplemental appendix 2). The information is entered into the Registry database within the electronic Hospital Information System of SKMCH&RC, developed in Oracle by the Information Technology staff.

Incidence date

The incidence date on the data capture form is defined as the date of cytological/histological confirmation of malignancy on a pathology report; the date of consultation at an outpatient clinic/walk-in clinic (without a clinical investigation or a tissue diagnosis); the date of clinical investigation(s) as imaging or tumour markers confirming the diagnosis; the date of admission to the hospital because of a malignancy; or the date of death if no information is available other than the fact that the patient has died because of a malignancy. The proportion of cases microscopically verified (MV%) is determined by including both the histologically confirmed cases and those diagnosed based on exfoliative cytology of the specimens.

Cancer coding

Cancers are coded using the International Classification of Diseases for Oncology, Third Edition,¹⁹ and further categorised using the International Classification of

Diseases, Clinical Modification, 10th edition.^{20 21} All malignancies with a behaviour code of /2 (in-situ) and /3 (malignant) and, /0 (benign) and /1 (borderline malignancy) for Central Nervous System (CNS) tumours (brain and nervous system), are included.^{20 21}

Edit checks

To check for consistency between items, data are submitted to the IARC-CHECK programme to examine the data applying the following edits: sex versus site/histology, age versus the date of birth, site versus morphology, site versus age, histology versus behaviour and histology versus the basis of diagnosis. A check for multiple primaries is done using the IARCcrgTools package, according to the rules developed.¹⁹ A check for duplicate records is done manually based on the patient's name, telephone number, father's name, age, address and primary site. If two or more variables match, records were further checked to find out if it is an actual duplicate or a subsequent primary. It has to be carried out in this way because most patients do not provide the computerised national identity card number, meant to be a unique personal identifier.

Study population

For our study, the residents of Lahore (district) were included. Using the last census data and a growth rate of 3.46%, the average annual population of Lahore was estimated at 11.1 million.²²

Study design and incidence rates

An incidence study was conducted based on the data collected over the years. Cancer counts were computed and crude incidence rates were categorised per 100 000 population by sex, cancer site/type, and 5-year age-group (0–5 until 70–74, then 75+), over 10 years. The rates computed were standardised using the Segi world standard and presented per 100 000 population.²³ Results were stratified by sex and age-group, that is, children (0–14 years), adolescents (15–19 years) and adults (≥20 years).

Analysis

Data sets were analysed using Microsoft Excel 2016 and IBM SPSS Statistics V.20.

RESULTS

An overview

The population pyramid shows the estimates for Lahore (figure 1). The average annual population of Lahore was estimated at 11 128 776. Nearly 40% were below age 15 years and males accounted for 52.6% of the total population. Over 10 years, 58 394 new malignancies were recorded in 58 287 patients due to double primaries seen in 107 patients. Female patients were predominant (57.1%), with a female-to-male ratio of 1.3:1. Almost 34% of the patients were in the 50–64 year age-group. Most of the patients were adults (92.2%), followed by children (5.6%) and adolescents (2.2%). Per 100 000 population,

Figure 1 Population pyramid showing average annual person-years by sex and age-group: Lahore, Pakistan, 2010–2019.

for all sites combined, the age-standardised incidence rate (ASIR) was 103.4 in females and 65.6 in males; among children, it was 6.1 and 8.9, in adolescents 8.6 and 11.4 and among adults 167.8 and 103.1, for females and males, respectively (figure 2).

ASIRs

Table 1 shows the ASIRs for children and young adults. Stratifying the results by age-group and sex, in terms of ranking, high ASIRs were seen for the following cancer sites/types: among children, in females, lymphoid leukaemia (1.6), brain/other nervous system (0.7) and eye (0.5), whereas, among males, lymphoid leukaemia (2.4), Hodgkin's lymphoma (1.0) and brain/other nervous system (0.9). In adolescents, relatively high ASIRs were seen for malignancies of the bone (1.2), brain/other nervous system (1.1), ovary (0.7) and CNS (benign tumours (0.7)) among females, whereas, in males, ASIRs for tumours of the bone (2.2), brain/other nervous system (1.5) and non-Hodgkin's lymphoma (NHL (1.4)) were comparatively high. Figure 3 shows the ASIRs for top-ranking cancers in children and young adults.

Table 2 displays the ASIRs for adults, by sex and cancer site/type. The highest rates recorded were as follows: among females, cancers of the breast (76.7), uterus (9.1), ovary (7.1), colorectum/anus 6.1 and lip/oral cavity (5.7), whereas, in males, prostate (10.7), bladder (8.0), trachea/bronchus/lung (7.6), colorectum/anus (7.6) and NHL (7.1). Uterine cancers included the corpus uteri, uterus unspecified and placenta. Figure 4 shows the ASIRs according to ranking, by sex, in adults.

Age-specific incidence rates

The age-specific incidence rates were higher for females than for males reaching a peak of 420 per 100 000 females in the 55–65 year age-group and 330 per 100 000 males in the 60–70 year age-group (figure 5). The age-specific incidence rates for leading cancer sites, by sex, are shown in figures 6–7 and online supplemental appendix 3.

Descriptive statistics

On exploring the data further, the following statistics were obtained for the age at diagnosis. For cancers in females (N=33 325), the mean age was 48.5±16.4 (0–106

Figure 2 Age-standardised incidence rates (ASIRs) by sex and age-category: Lahore, Pakistan, 2010–2019.

years), median and mode 50 years, and for breast cancer (14 975 cases), mean 50.1 ± 12.9 (7–94 years), and median and mode 50 years. In males (N=25 069), the mean age was 49.8 ± 20.5 (0–116 years), median 54 years, and mode 60 years and, for prostate cancer (1974 cases), mean 68.9 ± 9.8 (22–116 years), and median and mode 70 years.

DISCUSSION

ASIRs

Children and adolescents

During 2010–2019, in Lahore, among females (0–19 years), the ASIRs for cancers of the bone, ovary, brain/other nervous system including benign tumours, lymphoid leukaemia and eye were high. Among males, apart from tumours of the bone and brain/other nervous system, Hodgkin's lymphoma and NHL were in the top-ranking cancers (figure 3). Similar findings were reported in a recent publication from an institution in Rawalpindi, Pakistan.²⁴ Hodgkin's lymphoma could be attributed to poor nutrition and frequent exposure to infectious agents, including the Epstein-Barr virus (EBV), which has a proven role in its aetiology.²⁵ Both leukaemia and lymphoma shared the burden of haematological malignancies in this cohort of patients, accounting for nearly half of the malignancies. As for leukaemia, an abnormal karyotype was found in 48% of the children suffering from acute lymphoblastic leukaemia, in a study conducted in Karachi.²⁶ In another study, in acute myeloid leukaemia, nearly 25% of the patients showed the core-binding factor associated with translocations.²⁷ In the USA, recent germline genomic studies have revealed that at least 5%–10% of children with cancer and nearly 3%–4% with acute lymphoblastic leukaemia, develop the disease due to an underlying genetic predisposition.²⁸ Further, in a report from China, the two most important factors identified for childhood leukaemia are exposure to hydrocarbons and ionising radiation.²⁹ In another study from the USA, it has been reported that factors including birth weight, parental age and congenital anomalies are consistently associated with most types of paediatric cancer, while high dose ionising radiation and prior chemotherapy are accepted causes of childhood cancer, increasing the risk several times.³⁰ In yet another study, the main factors implicated in the pathogenesis of osteosarcoma include Paget's disease, hereditary retinoblastoma, Li-Fraumeni syndrome, antineoplastic drugs and ionising radiation, whereas, for Ewing's sarcoma, Caucasian race, parental

occupation, parental smoking and surgery for inguinal hernia.³¹ However, many of the aforementioned studies have not been conducted in Pakistan. Therefore, it is difficult to highlight the exact risk factors in our country.

Adults

Among females, high ASIRs for cancers of the breast, reproductive system, colorectum/anus and lip/oral cavity were seen (figure 4). The mean age at diagnosis for breast cancer (50 years) was lower than that seen in the USA, which was 62 years.³² This may also be attributed to a difference in the life expectancy between the two regions. In Pakistan, the life expectancy of females was estimated at 68, whereas, in the USA, at 81.2 years.^{1 33} The factors associated with the aetiology of breast cancer have been studied extensively but there is no consensus on a single factor implicated in its carcinogenesis. Most cancers are sporadic, without a family history of the disease.³⁴ However, both modifiable and non-modifiable factors as young age at menarche, single marital status, nulliparity, late first full-term pregnancy, use of oral contraceptives, late menopause, a family history of breast cancer and a high body mass index could be associated with an increased risk of developing the disease.⁷ Evolving a system using breast physicians would be worthwhile, given the fact that Pakistan is a densely populated, resource-constrained country, where setting up a formal screening programme and accessing healthcare are daunting tasks both for the healthcare providers and the public at large, respectively.³⁵ About cancers of the reproductive system, in a study on cervical cancer in Karachi, human papillomavirus (HPV) types 16 and 18 were found in 82.4% of invasive cervical cancer.³⁶ Therefore, HPV could be implicated in the aetiology of cervical cancer.

In males, comparatively high ASIRs were recorded for prostate, tobacco-related cancers (urinary bladder and lower respiratory tract) and colorectum/anus (figure 4). In the past, screening for prostate cancer using the prostate-specific antigen test has been advocated, globally; however, in recent years, the recommendations have underscored a patient-centred perspective, which de-emphasises public health and societal approaches.³⁷ Further, there is substantial evidence to suggest smoking and obesity as risk factors for prostate cancer; therefore, the emphasis should be on prevention rather than cure.³⁸ As for other tobacco-related cancers especially those of the urinary bladder, lower respiratory tract and lip/oral cavity, there is an urgent need to strictly reinforce the measures introduced for tobacco control.³⁹ Based on the WHO's standardised estimate of smoking prevalence, Pakistan is one of 15 countries worldwide with a heavy burden of tobacco-related ill-health; nearly 32% of men, 6% of women and 19% of Pakistan's adult population have been shown to use tobacco in one form or another.³⁹ Not only this, in recent years, a decline related to cigarette smoking with a concomitant increase in the use of various

Table 1 The age-standardised incidence rates (ASIRs) by sex and cancer site/type, in children and adolescents: Lahore, Pakistan, 2010–2019

Incidence rate→ Cancer site/type↓	ICD-10-CM* code	Children (0–14 years)			Children Boys			Adolescent (15–19 years)			Adolescent Males		
		N	%	Crude	ASIR	N	%	Crude	ASIR	N	%	Crude	ASIR
Lip	C00	1	0.1	0.0	0.0	0	0.0	0.0	0.0	1	0.1	0.0	0.0
Tongue	C01–C02	0	0.0	0.0	0.0	1	0.1	0.0	0.0	1	0.1	0.0	0.0
Mouth	C03–C06	3	0.2	0.0	0.0	5	0.3	0.0	0.0	1	0.1	0.0	0.0
Salivary glands	C07–C08	5	0.4	0.0	0.0	5	0.3	0.0	0.0	1	0.1	0.0	0.0
Tonsil	C10	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0
Nasopharynx	C11	4	0.3	0.0	0.0	10	0.5	0.0	0.0	13	2.5	0.2	0.3
Hypopharynx	C12–C13	0	0.0	0.0	0.0	0	0.0	0.0	0.0	1	0.2	0.0	0.0
Pharynx	C14	1	0.1	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0
Oesophagus	C15	0	0.0	0.0	0.0	0	0.0	0.0	0.0	4	0.8	0.1	0.0
Stomach	C16	0	0.0	0.0	0.0	1	0.1	0.0	0.0	2	0.4	0.0	0.0
Small intestine	C17	0	0.0	0.0	0.0	0	0.0	0.0	0.0	1	0.2	0.0	0.0
Colon	C18	8	0.6	0.0	0.0	4	0.2	0.0	0.0	16	3.0	0.3	0.2
Rectum	C19–C20	2	0.2	0.0	0.0	6	0.3	0.0	0.0	19	3.6	0.3	0.3
Anus	C21	0	0.0	0.0	0.0	1	0.1	0.0	0.0	2	0.4	0.0	0.0
Liver	C22	16	1.3	0.1	0.1	21	1.1	0.1	0.1	6	1.1	0.1	0.1
Gall bladder, etc	C23–C24	0	0.0	0.0	0.0	0	0.0	0.0	0.0	1	0.2	0.0	0.0
Pancreas	C25	0	0.0	0.0	0.0	0	0.0	0.0	0.0	2	0.4	0.0	0.0
Nose, sinuses, etc	C30–C31	2	0.2	0.0	0.0	3	0.2	0.0	0.0	2	0.4	0.0	0.1
Larynx	C32	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0
Trachea, bronchus, lung	C33–C34	5	0.4	0.0	0.0	1	0.1	0.0	0.0	6	1.1	0.1	0.1
Other thoracic organs	C37–C39	4	0.3	0.0	0.0	5	0.3	0.0	0.0	2	0.4	0.0	0.0
Bone	C40–C41	95	7.5	0.4	0.4	120	6.0	0.5	0.5	73	13.8	1.2	2.2
Melanoma of the skin	C43	1	0.1	0.0	0.0	1	0.1	0.0	0.0	0	0.0	0.0	0.0
Other skin	C44	6	0.5	0.0	0.0	14	0.7	0.1	0.1	4	0.8	0.1	0.1
Mesothelioma	C45	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0.0
Connective, soft tissue	C47, C49	70	5.5	0.3	0.3	82	4.1	0.4	0.4	29	5.5	0.5	0.6
Breast	C50	3	0.2	0.0	0.0	0	0.0	0.0	0.0	13	2.5	0.2	0.3
Vulva	C51	1	0.1	0.0	0.0	–	–	–	–	0	0.0	0.0	–
Vagina	C52	0	0.0	0.0	0.0	–	–	–	–	0	0.0	0.0	–
Cervix uteri	C53	1	0.1	0.0	0.0	–	–	–	–	2	0.4	0.0	–
Corpus uteri	C54	1	0.1	0.0	0.0	–	–	–	–	1	0.2	0.0	–
Uterus unspecified	C55	0	0.0	0.0	0.0	–	–	–	–	0	0.0	0.0	–

Continued

Table 1 Continued

Incidence rate →		Children (0–14 years)			Children Boys			Adolescent (15–19 years)			Adolescent Males			
Cancer site/type ↓	ICD-10-CM* code	N	%	Crude	ASIR	N	%	Crude	ASIR	N	%	Crude	ASIR	
Ovary	C56	42	3.3	0.2	0.2	-	-	-	-	42	7.9	0.7	-	-
Other female genital organs	C57	2	0.2	0.0	0.0	-	-	-	-	2	0.4	0.0	-	-
Placenta	C58	0	0.0	0.0	0.0	-	-	-	-	0	0.0	0.0	-	-
Penis	C60	-	-	-	-	0	0.0	0.0	0.0	-	-	-	0	0.0
Prostate	C61	-	-	-	-	0	0.0	0.0	0.0	-	-	-	0	0.0
Testis	C62	-	-	-	-	22	1.1	0.1	0.1	-	-	-	24	3.2
Other male genital organs	C63	-	-	-	-	1	0.1	0.0	0.0	-	-	-	0	0.0
Kidney	C64	53	4.2	0.3	0.3	78	3.9	0.3	0.4	3	0.6	0.0	5	0.7
Renal pelvis	C65	1	0.1	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Ureter	C66	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Urinary bladder	C67	4	0.3	0.0	0.0	6	0.3	0.0	0.0	2	0.4	0.0	2	0.3
Other urinary organs	C68	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Eye	C69	93	7.3	0.4	0.5	104	5.2	0.5	0.5	1	0.2	0.0	5	0.7
Brain, nervous system	C70–C72	160	12.6	0.8	0.7	207	10.4	0.9	0.9	67	12.7	1.1	100	13.5
Thyroid	C73	11	0.9	0.1	0.0	6	0.3	0.0	0.0	26	4.9	0.4	9	1.2
Adrenal	C74	2	0.2	0.0	0.0	7	0.4	0.0	0.0	0	0.0	0.0	1	0.1
Other endocrine	C75	1	0.1	0.0	0.0	4	0.2	0.0	0.0	3	0.6	0.0	3	0.4
Hodgkin's lymphoma	C81	64	5.0	0.3	0.3	242	12.1	1.1	1.0	37	7.0	0.6	65	8.8
Non-Hodgkin's lymphoma	C82–C86, C88.4, C96	87	6.9	0.4	0.4	193	9.7	0.9	0.8	25	4.7	0.4	88	11.9
Multiple myeloma	C90	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Lymphoid leukaemia	C91	332	26.1	1.6	1.6	522	26.2	2.3	2.4	17	3.2	0.3	36	4.9
Myeloid leukaemia	C92–94	47	3.7	0.2	0.2	85	4.3	0.4	0.4	21	4.0	0.3	26	3.5
Leukaemia unspecified	C95	56	4.4	0.3	0.3	110	5.5	0.5	0.5	10	1.9	0.2	11	1.5
Myelodysplastic syndrome	MDS	1	0.1	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Myeloproliferative disorders	MPD	0	0.0	0.0	0.0	0	0.0	0.0	0.0	0	0.0	0.0	0	0.0
Other & unspecified	O&U	52	4.1	0.2	0.3	67	3.4	0.3	0.3	22	4.2	0.4	49	6.6
Benign CNS	Other benign CNS	33	2.6	0.2	0.1	61	3.1	0.3	0.3	41	7.8	0.7	34	4.6
All sites		1270	100.0	6.0	6.1	1995	100.0	8.9	8.9	529	100.0	8.6	740	100.0

* ICD-10-CM: International Classification of Diseases, 10th edition, Clinical Modification.

†CNS: Central Nervous System.

CNS, Central Nervous System; ICD-10-CM, International Classification of Diseases, 10th edition, Clinical Modification.

Figure 3 Age-standardised incidence rates (ASIRs) by sex for leading cancer sites/types, in children and adolescents: Lahore, Pakistan, 2010–2019.

forms of smokeless tobacco products, including ‘naswar’ (powdered tobacco snuff), has also been noted.⁴⁰

The ASIRs for cancers of the gastrointestinal tract, liver, brain/other nervous system, skin and NHL were also ranked among the highest in Lahore, in both males and females. In a case–control study conducted in Karachi, a positive association has been suggested between colorectal cancer and a family history of cancer, a high-fat diet, weight loss, constipation, haematochezia, smoking and alcohol consumption.^{41–42} Sadly, Pakistan has the second-highest global burden of hepatitis C virus (HCV) infection, with 5% of the population infected (8 million people).⁴³ Delay in the diagnosis of HCV has resulted in chronic liver disease and hepatocellular carcinoma. The most important risk factor identified is the reuse of syringes for unnecessary therapeutic purposes.⁴³ For cancers of the brain/other nervous system, ionising radiation is a well-recognised risk factor but results for other factors such as industrial exposures, common mutagens of tobacco, dietary factors and alcohol are inconclusive.⁴⁴ NHL being among the leading malignancies in the region could be the result of an association with the oncogenic viruses.⁴⁵ In a study conducted in Islamabad, the EBV-1 DNA, confirming EBV presence in tissue samples, was detected in 82% of the samples, thus implicating EBV in the aetiology of lymphoma, both Hodgkin’s and NHL, with the proportion detected increasing with the age of the patients (6–83 years).⁴⁶ For skin cancer including melanoma, exposure to ultraviolet radiation could induce a suppressed immune environment for the initiation of carcinogenesis using complex pathways.⁴⁷ However, this area is yet to be explored in Pakistan.

Age-specific incidence rates

For all sites combined, the age-specific incidence rates were higher for females than for males (figure 5). Among females, there was an upward trend of the incidence rate for breast cancer starting at age 20, reaching the highest at 50–65 years (160 per 100 000), followed by a downward trend (figure 6). For cancers of the uterus, an upward trend was noticed at age 40 until 65 years (30 per 100 000), followed by a decline, whereas, for malignancies of the lip/oral cavity, an upward trend was noted at age 35 years (20 per 100 000) and it remained more or less stable, thereafter. Among males, the incidence rates for

prostate cancer started going up at age 40, reaching the highest at 70 years (90 per 100 000), whereas, cancers of the urinary bladder followed a similar pattern, reaching a peak of 37 per 100 000 (figure 7). Likewise, cancers of the lower respiratory tract started going up at age 40 years, reaching a peak at 60–70 years, followed by a slight decline.

Comparison with other regions

In table 3, a comparison of the ASIRs obtained for Lahore with the Globocan 2020 estimates for selected countries in Asia, and two other regions in Africa (Mauritius and Addis Ababa (Ethiopia)) has been made.^{48–50} In Pakistan, for both sexes combined, cancers of the breast, lip/oral cavity, lung, oesophagus, prostate, cervix uteri, colorectum, ovary, leukaemia and stomach were in the top 10 malignancies, according to the Globocan estimates. Among females, the ASIRs for breast cancer in the UAE (58.5), Mauritius (53.7) and Lahore (46.1) were higher than in other regions shown in the table. This is perplexing because these three regions are different from one another as regards geography, lifestyle and dietary habits. Further, India (25.8) and Iran (35.8) are Pakistan’s neighbouring countries but the ASIR for breast cancer was low in these regions compared with Lahore, as shown in the Globocan 2020 estimates.⁴⁸ The aforementioned plausible risk factors for breast cancer in Pakistan indicate that most cancers are sporadic. The ASIR for cancer of the cervix uteri was high in Addis Ababa (21.5), India (18.0) and Thailand (16.4), compared with Pakistan (6.1) and Lahore (2.5). This could be because of the presence of specific oncogenic types of HPV 16 and 18, in the development of cervical cancer. The HPV prevalence in the general population versus patients with cervical cancer has been documented as 10.5% versus 65% and 7.8% versus 80.3%, in the far east and southern Asia, respectively.⁵¹ The HPV prevalence, along with promiscuity and multiple sexual partners, contributed significantly to the development of the disease, leading to high incidence rates.

The ASIR for cancers of the lower respiratory tract was higher in Thailand (female (F) 11.9, male (M) 27.4) and Iran (F 8.1, M 16.9) than in other regions including Lahore (F 1.4, M 4.6); and for leukaemia, higher in Iran (F 6.0, M 8.9), and Addis Ababa (F 5.6, M 5.9), than in Lahore (F 1.8, M 2.3). Thailand is a land of cultural diversity. Although the smoking prevalence recorded in Thailand decreased from 32.0% in 1991 to 21.2% in 2007, it was still high, partly explaining the comparatively high lung cancer incidence rate in Thailand.⁵² The relatively high ASIR for leukaemia in Iran and Addis Ababa could be explained by a history of smoking or working with industrial or agricultural chemicals; benzene and formaldehyde are known cancer-causing chemicals found in tobacco smoke, building materials and household chemicals.⁵³

The ASIR for colorectal cancer was high in the UAE (F 17.3, M 11.5), Thailand (F 15.2, M 19.0) and Iran (F 11.9,

Table 2 The age-standardised incidence rates (ASIRs) by sex and cancer site/type, in adults: Lahore, Pakistan, 2010–2019

Incidence rate→		Adult females (≥20 years)				Adult males			
Cancer site/type↓	ICD-10-CM code	N	%	Crude	ASIR	N	%	Crude	ASIR
Lip	C00	35	0.1	0.1	0.2	53	0.2	0.2	0.2
Tongue	C01–C02	452	1.4	1.8	2.6	625	2.8	2.1	2.8
Mouth	C03–C06	499	1.6	2.0	2.9	849	3.8	2.9	3.8
Salivary glands	C07–C08	127	0.4	0.5	0.6	162	0.7	0.5	0.7
Tonsil	C10	21	0.1	0.1	0.1	34	0.2	0.1	0.2
Nasopharynx	C11	43	0.1	0.2	0.2	103	0.5	0.3	0.4
Hypopharynx	C12–C13	110	0.3	0.4	0.6	91	0.4	0.3	0.4
Pharynx	C14	16	0.1	0.1	0.1	20	0.1	0.1	0.1
Oesophagus	C15	376	1.2	1.5	2.1	520	2.3	1.8	2.5
Stomach	C16	381	1.2	1.5	2.0	576	2.6	1.9	2.6
Small intestine	C17	103	0.3	0.4	0.6	111	0.5	0.4	0.5
Colon	C18	577	1.8	2.3	3.2	882	3.9	3.0	4.0
Rectum	C19–C20	456	1.4	1.8	2.4	677	3.0	2.3	3.0
Anus	C21	100	0.3	0.4	0.5	129	0.6	0.4	0.6
Liver	C22	605	1.9	2.4	3.7	1144	5.1	3.9	5.7
Gall bladder, etc	C23–C24	464	1.5	1.8	2.8	311	1.4	1.0	1.5
Pancreas	C25	136	0.4	0.5	0.8	211	0.9	0.7	1.0
Nose, sinuses, etc	C30–C31	58	0.2	0.2	0.3	102	0.5	0.3	0.5
Larynx	C32	99	0.3	0.4	0.6	706	3.2	2.4	3.5
Trachea, bronchus, lung	C33–C34	400	1.3	1.6	2.3	1463	6.6	4.9	7.6
Other thoracic organs	C37–C39	43	0.1	0.2	0.2	97	0.4	0.3	0.4
Bone	C40–C41	146	0.5	0.6	0.6	236	1.1	0.8	0.8
Melanoma of the skin	C43	41	0.1	0.2	0.2	46	0.2	0.2	0.2
Other skin	C44	695	2.2	2.7	4.1	962	4.3	3.2	4.5
Mesothelioma	C45	5	0.0	0.0	0.0	6	0.0	0.0	0.0
Connective, soft tissue	C47, C49	293	0.9	1.2	1.4	364	1.6	1.2	1.5
Breast	C50	14 671	46.5	57.9	76.7	286	1.3	1.0	1.4
Vulva	C51	58	0.2	0.2	0.3	–	–	–	–
Vagina	C52	61	0.2	0.2	0.3	–	–	–	–
Cervix uteri	C53	774	2.5	3.1	4.1	–	–	–	–
Corpus uteri	C54	1173	3.7	4.6	7.1	–	–	–	–
Uterus unspecified	C55	324	1.0	1.3	1.9	–	–	–	–
Ovary	C56	1375	4.4	5.4	7.1	–	–	–	–
Other female genital organs	C57	90	0.3	0.4	0.5	–	–	–	–
Placenta	C58	16	0.1	0.1	0.1	–	–	–	–
Penis	C60	–	–	–	–	11	0.0	0.0	0.0
Prostate	C61	–	–	–	–	1974	8.8	6.7	10.7
Testis	C62	–	–	–	–	270	1.2	0.9	0.8
Other male genital organs	C63	–	–	–	–	11	0.0	0.0	0.1
Kidney	C64	336	1.1	1.3	1.8	578	2.6	1.9	2.7
Renal pelvis	C65	4	0.0	0.0	0.0	12	0.1	0.0	0.1
Ureter	C66	2	0.0	0.0	0.0	3	0.0	0.0	0.0
Urinary bladder	C67	372	1.2	1.5	2.3	1574	7.0	5.3	8.0
Other urinary organs	C68	3	0.0	0.0	0.0	5	0.0	0.0	0.0

Continued

Table 2 Continued

Incidence rate→ Cancer site/type↓	ICD-10-CM code	Adult females (≥20years)				Adult males			
		N	%	Crude	ASIR	N	%	Crude	ASIR
Eye	C69	51	0.2	0.2	0.3	79	0.4	0.3	0.4
Brain, nervous system	C70–C72	798	2.5	3.1	3.7	1474	6.6	5.0	5.8
Thyroid	C73	684	2.2	2.7	3.0	279	1.2	0.9	1.1
Adrenal	C74	13	0.0	0.1	0.1	10	0.0	0.0	0.0
Other endocrine	C75	1	0.0	0.0	0.0	6	0.0	0.0	0.0
Hodgkin's lymphoma	C81	211	0.7	0.8	0.9	434	1.9	1.5	1.6
Non-Hodgkin's lymphoma	C82–C86, C88.4, C96	990	3.1	3.9	5.5	1611	7.2	5.4	7.1
Multiple myeloma	C90	122	0.4	0.5	0.7	165	0.7	0.6	0.8
Lymphoid leukaemia	C91	87	0.3	0.3	0.4	154	0.7	0.5	0.6
Myeloid leukaemia	C92–94	241	0.8	1.0	1.1	307	1.4	1.0	1.2
Leukaemia unspecified	C95	61	0.2	0.2	0.3	66	0.3	0.2	0.2
Myelodysplastic syndrome	MDS	1	0.0	0.0	0.0	6	0.0	0.0	0.0
Myeloproliferative disorders	MPD	5	0.0	0.0	0.0	9	0.0	0.0	0.0
Other & unspecified	O&U	1970	6.2	7.8	11.1	1833	8.2	6.2	8.6
Benign CNS	Other benign CNS	751	2.4	3.0	3.4	697	3.1	2.3	2.6
All sites		31 526	100.0	124.4	167.8	22 334	100.0	75.3	103.1

CNS, Central Nervous System; ICD-10-CM, International Classification of Diseases, 10th edition, Clinical Modification.

M 15.9) compared with Lahore (F 3.7, M 4.6) while that for liver cancer it was again high in Thailand (F 12.9, M 33.8) and Iran (F 6.1, M 7.5) relative to Lahore (F 2.2, M 3.5). The ASIR for thyroid cancer was high among females in the UAE (12.5), Thailand (6.4) and Iran (6.7) in comparison with their male counterparts and for Lahore (F 1.8). The clinicopathological heterogeneity further complicates the divergent biological behaviours of these tumours.

Although the ASIR for all sites and age-groups combined among males was low in Lahore (65.6), it was also low for males in Addis Ababa (70.7). This is also based on the first report of its kind released from the Addis Ababa Registry.

A difference in the ASIRs of lip/oral cavity, cervix uteri and ovary between Lahore and Pakistan has been explored further. It could be attributed to the fact that for all cancers combined, the Globocan estimates are based on the incidence rates obtained by averaging overall rates from neighbouring countries and then partitioning them to obtain the national incidence rates for specific sites.⁵⁴

Figure 4 Age-standardised incidence rates by sex for leading cancer sites/types, in adults: Lahore, Pakistan, 2010–2019.

Recent results for the Karachi division in Pakistan, representing a population of nearly 16 million, show a preponderance of tobacco-related cancers and breast malignancies among adults.⁴ The ASIR for oral cancers was 42.8 in adult males and 76.1 for breast cancer among adult females, whereas bone tumours and leukaemia were common in children and young adults.⁴ A high ASIR for oral cancers is attributed to excessive consumption of naswar (a powdered form of tobacco), used intranasally or buccally.⁴

Even though researchers/clinicians in Pakistan have attempted to explore potential risk factors implicated in the aetiology of different types of cancers within the study population(s) of a hospital or an institution, there is a pressing need to study risk factors more extensively within

Figure 5 Age-specific incidence rates by sex: Lahore, Pakistan, 2010–2019.

Figure 6 Age-specific incidence rates for leading cancer sites/types in females: Lahore, Pakistan, 2010–2019.

a predefined population in a geographically demarcated area, over a specified time. A study of risk factors could assist in explaining a difference in the incidence rates by cancer type in the region.

Data quality

The data presented are comparable to the data presented by registries in the developed regions of the world in terms of the systems used for classifying and coding neoplasms, the definition of incidence date and the rules for dealing with multiple primaries. However, evaluating the completeness, that is, the extent to which all the incident cancers occurring within the population of Lahore were included in the Registry database, is difficult at this stage. Nevertheless, it is hoped that it will be possible over time as the Registry matures, and the results are collated.

Figure 7 Age-specific incidence rates for leading cancer sites/types in males: Lahore, Pakistan, 2010–2019.

According to the proportion of cases microscopically verified, among females, between 88% and 99%, whereas, in males, 92%–99% were MV%, except for liver cancer in either sex where nearly 50% of the cases were morphologically verified. As a measure of validity, these figures appear to be reasonable except for cancers of the brain/other nervous system, lung/trachea/bronchus, gastrointestinal system and leukaemia.⁵⁵ However, over the years, it will be determined if the figures change. The mortality-to-incidence ratio could not be computed either because no centralised system exists for gathering mortality data in the region. The absence of a death registry also contributed to the failure to capture the ‘death certificate only’ cases.

Further, the age-specific incidence rates did not show any abnormal fluctuations in the anticipated patterns.

Generalisability of the results

Regarding the generalisability of the results shown, a lot needs to be taken into consideration. Pakistan has 150 districts as its administrative units while the district of Lahore is one of the 36 districts in Punjab.⁵⁶ Further, the Lahore district represents nearly 1/20th of the population of the country and 1/10th of the population of the province.⁵⁷ Given that, at present, adequate and updated information is not available to stratify populations of various districts by age-group, sex, marital status, race/ethnicity, occupation and urban–rural divide, it is debatable if the results can be extrapolated to the population of the province or country. Moreover, the results presented in this manuscript are based on the current study and there are no historical data to compare the results with. Therefore, it is not possible to gauge the extent of under-reporting.

Healthcare delivery

On average, 5800 new cancer cases were diagnosed in Lahore every year. This being a significant number, a review of the cancer facilities in the region has been done. It shows that cancer continues to be largely a surgical disease in Pakistan, with most patients presenting to, and being managed by, surgeons in the first instance.⁵⁸ However, this goes side by side with the fact that the principles of oncologic surgery are not widely known. Therefore, it would be reasonable to commence programmes based on such principles in various hospitals of the region.⁵⁸ Further, the Pakistan Atomic Energy Commission has established 17 hospitals in the country since it started functioning in the 1960s. At present, they deliver both radiation treatment and chemotherapy but do not have any diagnostic, surgical or palliative care services.^{7 58} Such hospitals tend to be under-equipped and see many more patients than is ideal for the facilities available.⁵⁸ Moreover, medical oncology was recognised as a separate field in the 1980s but paediatric oncology, as a distinct field, has only begun to develop over the last two decades. Despite this, there is a dearth of trained oncologists, and most patients with cancer never get to see a medical oncologist throughout their treatment.⁵⁸ The aforementioned

Table 3 Comparison of the age-standardised incidence rates in Lahore, Pakistan, with other regions

	Globocan estimates: Pakistan	UAE	Thailand	Iran	India	Current study: Lahore	Other reports: Mauritius	Addis Ababa, Ethiopia
Time period	2020	2020	2020	2020	2020	2010–2019	2011–2015	2012–2013
Population	220 892 332	9 890 400	69 799 978	83 992 953	1 380 004 378	11 128 776	123 300	30 490 000
ASIR in females	113.7	170.9	159.0	139.0	99.3	103.4	151.2	136.2
Breast	34.4	58.5	37.8	35.8	25.8	46.1	53.7	40.6
Corpus uteri	3.5	11.7	7.6	3.5	2.4	5.4	7.7	2.9
Ovary	5.1	6.5	7.9	4.4	6.7	4.4	5.7	8.5
Colorectum, anus	4.4	17.3	15.2	11.9	3.7	3.7	13.2	7.3
NHL	3.0	5.9	5.6	3.2	2.1	3.5	1.9	4.5
Lip, oral cavity	7.0	1.8	3.0	1.3	4.6	3.4	3.4	2.9
Skin*	–	–	–	–	–	2.5	–	4.9
Cervix uteri	6.1	6.2	16.4	2.3	18.0	2.5	11.2	21.5
Brain, nervous system	2.1	2.2	2.5	6.4	1.7	2.5	2.7	1.0
Liver†	3.1	3.2	12.9	6.1	1.6	2.2	1.9	3.0
Leukaemia	3.6	6.1	4.9	6.0	3.1	1.8	3.5	5.6
Thyroid	2.0	12.5	6.4	6.7	2.1	1.8	2.0	4.2
Gall bladder‡	2.8	1.1	1.2	0.8	1.9	1.7	–	–
Lung§	2.7	5.2	11.9	8.1	3.1	1.4	4.3	2.7
Bladder	1.0	3.7	1.8	1.9	0.7	1.4	1.3	1.5
Oesophagus	6.4	1.0	0.9	3.5	3.4	1.2	1.5	3.8
Stomach	3.6	4.1	3.1	12.5	2.9	1.2	4.4	2.6
Kidney	1.4	2.8	1.2	1.4	1.0	1.2	1.4	2.0
Pancreas	0.3	2.8	1.8	2.9	0.7	0.5	2.1	–
Larynx	0.9	0.4	0.3	1.2	0.7	0.3	–	0.1
ASIR in males	107.0	82.5	173.1	165.0	95.7	65.6	132.8	70.7
Prostate	6.3	13.4	14.6	21.2	5.5	6.4	16.5	6.4
Bladder	5.1	7.8	6.0	10.1	2.5	4.8	5.1	3.9
Lung	11.2	7.4	27.4	16.9	7.8	4.6	13.0	3.7
Colorectum, anus	6.2	11.5	19.0	15.9	6.0	4.6	17.0	7.9
NHL	4.7	4.4	7.4	5.1	3.2	4.6	3.6	6.8
Lip, oral cavity	13.2	1.5	5.1	1.4	14.8	4.1	7.7	3.5
Brain, nervous system	3.0	2.1	3.3	8.0	2.8	3.9	3.1	1.2
Liver	3.8	2.8	33.8	7.5	3.6	3.5	3.4	2.5
Skin	–	–	–	–	–	2.7	–	2.6
Leukaemia	5.0	4.9	6.1	8.9	4.2	2.3	4.6	5.9
Larynx	4.8	1.5	2.9	4.5	4.5	2.1	–	0.7
Kidney	1.8	2.2	2.7	2.4	1.6	1.8	2.5	0.9
Stomach	4.8	4.7	4.0	22.4	6.1	1.6	8.4	3.1
Oesophagus	6.6	0.9	5.3	4.6	6.1	1.5	3.8	2.3
Gall bladder	1.1	0.2	1.8	0.6	1.0	0.9	–	–
Breast	–	–	–	–	–	0.8	1.1	3.2
Thyroid	0.9	2.1	1.4	2.0	0.8	0.7	1.1	1.4

Continued

Table 3 Continued

	Globocan estimates: Pakistan	UAE	Thailand	Iran	India	Current study: Lahore	Other reports: Mauritius	Addis Ababa, Ethiopia
Pancreas	1.1	2.2	3.5	4.7	1.2	0.6	3.2	–

*Skin: includes non-melanoma cancers.

†Liver: includes the intrahepatic bile ducts.

‡Gall bladder: includes the extrahepatic bile ducts.

§Lung: includes trachea, bronchus and lung.

ASIR, Age-standardised incidence rate (per 100 000 population); NHL, non-Hodgkin's lymphoma.

issues are compounded by the fact that Pakistan being a populous country, the delivery of healthcare continues to be complex with a large proportion of the inhabitants being served through a mixed system via multiple health-care providers.⁵⁹ At the same time, cancer registration is a neglected area in the country and the problem is multifaceted: limited local awareness about this subject, a dearth of specialists required to work as coders/registrars and insufficient dedicated staff available to focus on the field. Moreover, existing cancer registration personnel are encumbered with infectious disease surveillance such as COVID-19. This situation is exacerbated by a reluctance to accept the negative consequences caused by the above factors, resulting in an overworked workforce.

CONCLUSIONS

Limited resources in Pakistan along with endemic, epidemic and pandemic infectious diseases and a population explosion have markedly delayed establishing systems already well established in the more developed regions of the world. The current study is an important one as it is the first time that an extensive 10-year report on population-based registration and incidence rates has been conducted. The existing literature indicates a lack of information related to population-based cancer registration and corresponding incidence and mortality statistics in various regions of Pakistan. The capture of mortality data is even harder than the incidence data as it is difficult to establish contact with many patients once they leave the facility where they are being taken care of.⁶⁰ Hospital administrators should consider establishing contact with the National Database and Registration Authority, to develop an agreement enabling the Registry to obtain death certificates (based on a list of patients with cancer provided).

Multifaceted methods including legislation and education of the public and clinicians using the Punjab Registry as the foundation could help establish more regional cancer registries and facilitate data capture, including mortality and survival data. This can be possible if cancer registration is considered one of the health priorities in Pakistan. Once the incidence and prevalence are estimated in larger populations, logistical issues such as training of oncologists, surgeons, pathologists, nurses and public health officers, along with the construction of

an adequate number of hospitals could be dealt with as a continuum of care. Point-of-care testing could also be explored to facilitate better disease diagnosis, monitoring and management. It is hoped that this study will draw the attention of policymakers and their progressive approach will bring about a positive and sustainable change in cancer registration in the region for years to come.

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Contributors FB conceived the idea of the study, analysed the data, interpreted the results, created the graphs, did the literature review and prepared and finalised the manuscript. SM checked the data for its validity and duplicate registrations, calculated the rates and prepared the tables.

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was submitted for conducting this retrospective study. The study was approved by the IRB (reference no. EX-20-12-19-01).

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ORCID iD

Farhana Badar <http://orcid.org/0000-0001-5600-1959>

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