RESEARCH COMMUNICATION

Toward Prostate Cancer Early Detection in Iran

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Abstract

Background: The aim of this study was to document the epidemiological features of prostate cancer in Iran and to define its public health priorities for an early detection program. Methods: A review of published articles from 1975 to October 2008 was conducted using different search engines and 147 Persian medical journals. Abstracts only were excluded. Inclusion criteria were studies on prostate cancer clinical and epidemiological data. Results: In all, 40 full texts, 7 national reports, and 10 provincial reports were accessed. The incidence rate of prostate cancer was 9.6 (3.2 to16.0) per 100,000 in multi geographical settings. The crude prostate cancer mortality rate was 4.5 per 100.000 in 2004. The prevalence of prostate cancer among patients with benign prostate hyperplasia (BPH) presentation was 6.3%. The overall prostate cancer detection rate was reported 3.6% in male over 40 years old by population screening programs. Conclusion: The rate of prostate cancer incidence in Iran is significantly less than those in developed countries and similar to Eastern Mediterranean Regions. However, it is expected to rise dramatically in the future because of the anticipated increase in life expectancy and percentage of old age groups. Therefore, prostate cancer control should be integrated into the National Cancer Control Program focusing on prevention and early detection in men over 40 years old or with symptomatic BPH. An appropriate PSA cut off point for screening should be defined by population pilot studies.

Key Words: Prostate cancer - early detection - Iran

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Introduction

Cancer is the third cause of death in Iran after coronary heart disease, accidents and other phenomenon (Naghavi, 2007) and prostate cancer is the third most common cancers among male in Iran. However, the trend of this cancer was not defined; its percentage has been increased more than three times (Mousavi et al., 2008) since 1975 to now. Currently there is no evidence from randomized controlled trials to demonstrate an increased survival resulting from intervention for early stage prostate carcinoma; therefore population screening is not currently recommended in most countries. The population screening program that showed decrease in prostate cancer mortality (up to 40–50%) came from the Tyrol region of Austria, where screening has been freely available for over a decade(Bartsch et al., 2005; Horninger et al., 2005).

The Asian countries where due to their relatively lower incidence; the concept of screening for prostate cancer did not emerge until recently except in Japan, where prostate cancer screening began as early as 1975 (Watanabe, 2001), in China in 1998 (Zhao et al., 2003; Gao et al., 2005), and in South Korea in 2007 (Song et al., 2008).

Prostate cancer control program has not been developed in Iran. Therefore this study was carried out to document the clinico-epidemiological features of prostate cancer, finding literature gaps and define public health priorities for prevention and early detection in Iran.

Materials and Methods

A comprehensive search was conducted to review of published articles from 1975 to October 2008. As the first report of prostate cancer was published in 1975 (Habibi, 1975); this year was selected as starting point. Different search engines were used including: PubMed (http://www.ncbi.nlm.nih.gov/sites/entrez last access Oct.2008), SID (http://www.sid.ir/fa/index.asp last access Oct.2008) and IranMedex (http://www.iranmedex.ir last access Oct.2008).

The following terms were used in the PubMed Database search: “Prostate cancer” was combined with the word “Iran” in their titles and abstracts. The search was repeated by replacing “cancer” with “carcinoma”, “malignancy” and “tumor”. Persian terms for prostate cancer were used in SID and IranMedex Databases search.

Hindering efforts to gather all published articles, particularly those published in Persian medical journals was the fact that they did not have a completed citation

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Table 1. Incidence of Prostate Cancer in Iran; Based on Geographical Settings

Geographical setting	Method base	Year	Population	Incidence Rate per 100,000 male population									Crude Rate	ASR	% T*
				40-4	45-9	50-4	55-59	60-4	65-9	70-4	75-79	80-84	>85			
National Cancer Registry Program																
Iran	Pathology	2003-2006	68,856,536	0.3	1.5	11.5	14.9	31.3	50.3	115.4	122.8	263.0	132.0	7.8	9.6	8.3
Ardebil	Population	2006	12,60,000	0.0	6.9	0.0	0.0	16.7	25.7	46.6	77.2	75.8	0.0	3.3	3.9	3.4
Golestan	Population	2006	1,622,879	2.3	5.3	13.6	9.9	25.9	39.9	115.9	130.0	235.8	119.0	7.4	9.3	6.4
Isfahan	Population	2006	4,008,234	0.8	2.9	8.3	18.0	49.0	87.7	172.5	201.5	593.9	319.0	12.9	16.0	10.7
Kerman	Population	2006	2,001,874	1.6	1.8	6.2	3.4	5.9	17.0	69.3	34.2	80.5	162.0	3.4	4.4	4.3
Lorestan	Population	2006	1,736,179	0.0	2.4	4.2	22.8	4.0	32.3	107.1	147.9	381.4	183.0	7.3	8.9	7.1
Provincial Cancer Registry Programs																
Ardebil	Population	1996-1999	1,128,864	1.0		2.5		7.9					34.8	2.2	3.4	2.6
Golestan	Population	2006	1,640,200	1.0		3.0		18.0					139.5	7.3	11.7	6.0
Kerman	Population	1996-2000	2,004,328	0.4		0.8		8.9					32.8	2.4	3.2	3.7
5 provinces	Population	1996-2000	NA	0.3		2.2		11.3					55.0	4.1	5.1	NA
Semnan	Population	1997-2001	293,000	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	8.2	10.1	6.6
Tehran	Population	1998-2001	7,427,901	O.5	1.1	5.1	15.5	36.5	95.2	145.7			365.5	10.3	15.5	8.5

%T*, percentage of all cancers in males; NA: Not available

Table 2. Prevalence of Prostate Cancer among BPH

Author	Year	Location	BPH	Cancer	%
Jebelameli	NA	Tehran[1]	124	12	9.7
Jamali Zavarehi	1981-1991	Tehran[2]	542	46	8.4
		Tehran[3]	150	13	8.6
		Yazd (S)	393	48	12.2
Babolhavaeji	1986-1996	Hamadan (NW)	1,192	57	4.8
Salehi	1994-1998	Rasht (N)	632	28	4.4
Falahatkar	2000-2002	Rasht (N)	1,398	75	5.4
Total			4,431	279	6.3

NA: Not available; [1]Sina Hospital; [2]Imam and [3]Markaze Pezeshki Hospital; S, South; NW, Northwest; N, North

index; many of them were searched by hand. Several authors were asked to provide us by submitting copies of their published manuscripts. Over 4,000 issues of 147 Persian medical journals were assessed manually from Medical College Library of Tehran University, Iran University Reference Medical Library and Central Library of Tabriz University of Medical Sciences. In addition, references cited in the identified articles were searched manually. Unpublished information and abstract books of scientific meetings were not included in this review. There was no hypothesis for statistical testing. Pooling was computed to estimate the prevalence of prostate cancer among patients with BPH. A range of data has been used for presenting the findings. These articles were classified into the categories of its epidemiological and clinical aspects.

Results

There were 46 citations in Medline, 48 in IranMedex, and 14 in the SID databases. Amongst them, 35 articles were published in Persian. Non-relevant publications and repeated articles were excluded from the analysis. Forty full text articles were included. Seven national reports, ten provincial reports and one dissertation on cancer registry in five provinces in Iran (Fallah, 2007) have been reviewed.

Incidence and prevalence rates

Incidence rate of prostate cancer was reported 9.6 (3.2 to 16) per 100.000 among Iranian male. The details are shown in Table 1. Adenocarcinoma was the most common morphology (97%). Table 2 summarizes data for studies carried out from 1981 to 2002. The prevalence of prostate cancer among patients with BPH presentation was 6.3% (4.4 to 12.2). The stage of prostate cancer and Gleason score was not reported.

Mortality rate

Prostate cancer was reported as the seventh most common underlying cause of cancer mortality, it was estimated 1550 deaths annually, crude mortality rate was 4.5 per 100.000 in 2004 (Naghavi, 2006) and its burden was reported 10,864 deaths in 2004 (Basiri et al., 2008).

Risk Factors

A study from 2005 to 2007 reported aging, sexual intercourse more than two times per week, elevated serum estradiol, and increasing fat consumption were the main risk factors for prostate cancer; and elevated serum testosterone, history of diabetes, and increased lycopene consumption were its protective factors (Pourmand et al., 2007).

Diagnostic and Screening Modalities

Three studies were carried out to evaluate the AgNOR staining for differentiating between hyperplasia and adenocarcinoma of prostate, all of them reported this staining might be a valid method for the diagnosis (Omidi

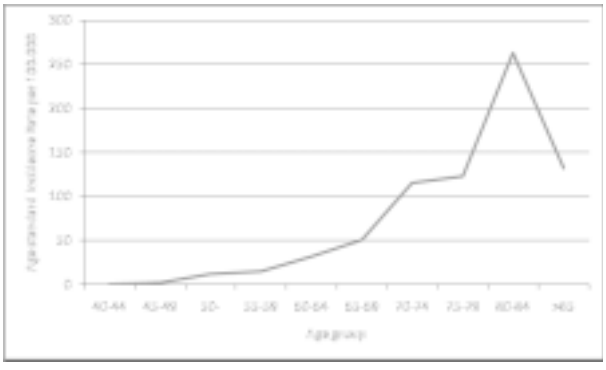

Figure 1. World Population Age Standard Incidence Rate of Prostate Cancer per 100,000 Male Population in Iran in 2006

et al., 2001; Parvin et al., 2001; Rajabi et al., 2001). Two population-based studies for PC screening were carried out: the first one from 1996 to 2004; by using PSA-based screening on 3670 Iranian men older than 40 years have been found the overall cancer detection rate 3.5% (Safarinejad, 2006), and the second study reported the overall cancer detection rate 3.6% by the same method on 3758 Iranian men over 40 years old from 2003 to 2005 (Hosseini et al., 2007).

Knowledge, attitude and practice of Iranian male on prostate cancer prevention were reported 55%, 40%, and 7% respectively (Rezaeian et al., 2006). The role of gelatinase A (MMP-2) on monitoring and screening patients with prostate cancer was reported as a promising procedure (Khorramizadeh et al., 2005).

Molecular and genetic epidemiology

Twenty one reports studied the molecular and genetic aspects of prostate cancer in Iran. Androgen receptor expression showed no prognostic value regarding its correlation with stage and differentiation status of the prostate carcinoma but it might be contributed to tumor cell progression (Amirmoghofran et al., 2004). Apoptosis was reported in 12% of 50 paraffin blocks of prostate cancers (Amirmoghofran et al., 2005). A study on 150 prostate cancer specimens showed 13.3% were positive for HER-2 gene over expression; the Gleason score was not different between HER-2-postitive and HER-2 negative patients (Mofid et al., 2007).

P53 protein expression was evaluated on 50 paraffin embedded tissue of prostate cancer and was found a significant association between this gene expression and differentiation status of prostate cancer (Gholijani et al., 2004). A study on 51 formalin-fixed paraffin-embedded specimens of prostate cancer showed PTEN mutation had a significantly greater Gleason score, poorer prognosis, and higher rate of metastasis (Pourmand et al., 2007).

There are some reports on the other aspects of prostate cancer such as: heat shock protein 70 in the thermoresistance of prostate cancer cell line spheroids (Khoeia et al., 2004), down-regulation of Hsp27 (Teimourian et al., 2006), immunosuppression by antigrowth cell factor (Abolhasani et al., 2004), metalloproteinase-2 (Shariftabrizi et al., 2005), neuroendocrine cells (ChA positive cells) (Afshar Moghaddam et al., 2006), expression of PI3K isoforms (Soheili et al., 2006), piezoelectric effect (Ghabili et al., 2008), basal membrane changes and reticular fiber distribution (Kermani et al., 2004), silibinin on the viability, migration and adhesion of the human prostate adenocarcinoma cell line (Mokhtari et al., 2008), TGIFLX/Y mRNA expression (Ousati Ashtiani et al., 2008), inhibition of chemomigration of human prostatic carcinoma cell line (TSU-pr1) by inhibition of epidermal growth factor receptor function (Zolfaghari et al., 1996), Insulin Growth Factor Receptor (Jalal et al., 2007), prostate cancer Protein Mass Spectra (Assareh et al., 2007).

Prostate Specific Antigen (PSA)

The results of sixteen studies on PSA in Iran were published in medical journals. There is no population based study to define the cut off point for PSA, besides a study in Yasuj (South of Iran) from 2003 to 2004 which carried out on 650 randomly selected men over 40 years old who had been referred to the Yasuj hospitals for a blood cell count; reported the PSA levels in the 95th percentile: 1.35 ng/mL, 1.85 ng/mL, 3.2 ng/mL, and 4.4 ng/mL for men aged 40 to 49, 50 to 59, 60 to 69, and older than 69 years, respectively, and mean serum PSA levels were 0.7 ng/mL, 0.9 ng/mL, 1.6 ng/mL, and 2.2 ng/mL, respectively (Mehrabi et al., 2005).

Clinical and survival studies

Seven articles described the clinical aspects of prostate cancer in Iran. Of them, a study on 42 cases of hormone refractory PC reported the combination of docetaxel, estramustine, and suramin might be highly effective regimen after a median follow-up of 23.4 months; they found the median time to progression was 57 weeks and median overall survival was 132 weeks (Safarinejad, 2005).

Another report studied the safety and efficacy of sorafenib in patients with castration resistant prostate cancer; sixty-four chemotherapy and radiotherapy cancer patients were intervened with this drug. It was shown the median overall survival was 14.6 months and no complete response occurred (Safarinejad, 2008).

Discussion

This report presented prostate cancer clinico-epidemiological data for the period 1975 to 2008. A major problem in this review was the fact that there is not a completed citation index for published articles in Persian medical journals. Most of the data was therefore unavailable in articles to allow for appropriate documentation; therefore some published articles might be missed for reviewing.

According available data, the trend of prostate cancer incidence was not defined; however in comparison with the report on 1975, the percentage of prostate cancer to total cancer among males has been increased more than three times. Annual report of Cancer Institute of New Salts Wales (NSW)-Australia reported prostate cancer has increased from 12% of all cancers in 1972 to 31% in 2005 (Tracey , 2007), the data of prostate cancer in Iran is more like to the 1972 in NSW.

Based on the transition of Iranian population, the children population (0-14 Years old) decreased from 44.5% in 1976 to 25.1% in 2006 while the persons aged 65 and over increased from 3.5% to 5.2% in 2006 and moreover it is expected the old aged population rise to highest number until 2050 (http://www.sci.org.ir/portal/faces/public/census85 last access Oct.2008); it is estimated the percentage of prostate cancer could be increased up to 30% of total cancer in male on that time.

According to the published data of Middle East Cancer Consortium (MECC) on cancer incidence in four member countries (Cyprus, Egypt, Israel, and Jordan) over the period 1996-2001; Cancer of the male genital system (mostly prostate) accounted for as little as 4%-10% of

male cancers in Egyptians, Jordanians, and Israeli Arabs, compared with 19%-33% in Israeli Jews, Cypriots, population (MECC, 2005); It was significantly less than European incidence rates (http://info.cancerresearchuk.org /cancerstats/types/prostate/incidence/#source13 last accessed Oct.2008), and US Surveillance, Epidemiology, and End Results (SEER) from 1975 to 2005 (http:// seer.cancer.gov/csr/1975_2005/results_merged/ sect_23_prostate.pdf last access Oct.2008- Jemal , 2008). This difference might be due to the underreporting, non diagnosed cases or lack of national screening or early diagnosis program (the availability of PSA testing (IARC , 2008) for prostate cancer in Iran.

Figure 1 shows an overall increasing trend for age peaking at age 80-84 with a significantly declining trend for men older than 84 years old in 2006. This pattern was reported for other cancers in Iran (Mousavi et al., 2008). Case ascertainment methods, data collection and sources of information, and misdiagnosed cases over 85 years old might be part of factors.

The incidence rates in Tehran (capital city) were slightly higher than the other provinces in Iran. The differences between the provinces incidence rates were significant. It might be due to the differences on the method for cancer registration, capture the data from referral hospitals, the diagnosis and reporting and the geographical setting.

According to the results of two population based screening for prostate cancer, the cancer detection rate was 3.5%; other studies for investigating the malignancy among BPH patients found over 6% of prostate cancer among them, these high prevalence reports might be due to the lack of screening program. It is compatible with other reports in developed countries during the last decades (Babaian, 1992- Bretton, 1994) and the same as the result of prostate cancer screening program in Korea in (Zhao et al., 2003) but much less than China in 1998 (Li et al., 2004). The prostate cancer crude mortality rate was significantly less than other reports (i.e. SEER with a rate of 33 per 100.000). The time trend was not reported because the lack of data in the past.

The studies on prostate cancer molecular and genetic were multidimensional, separated, and non-organized researches; since the costs of these studies might be high, these series of research should be linked to other relevant studies to find specific goals.

The survival rate of prostate cancer was not reported in Iran. Little clinical trials were carried out; the risk factors for prostate cancer were not still completely explained. Those could be some example gaps on prostate cancer research in Iran.

It is concluded that fighting against cancer, especially prostate cancer should be a governmental priorities in the country. Governmental supports to implement the Comprehensive National Cancer Control Program (CNCCP) are highly recommended (Mousavi et al., 2008). The prostate cancer control should be integrated in this program by focusing on prevention and early detection. Although on currently available evidences, population screening cannot be recommended, early detection in over 40 year old men or symptomatic BPH is highly recommended. The PSA cut off point should be defined by population based studies and the method for early detection and referring the suspected case should be clarified; the cost benefit and cost effective of this method should be assessed by pilot studies before integrating this program in the CNCCP. The local clinical trials should be supported to provide the evidence for the next 5–10 years in the area of prostate cancer treatment and use existing experts consensus for patient treatment at the present time for an urgently strategy to provide its national guideline protocol for treatment.

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