

## Incidence, Gleason Score and Ethnicity Pattern of Prostate Cancer in the Multi-ethnicity Country of Iran During 2008-2010

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**Purpose:** To investigate the geographical incidence, and grade of prostate cancer in Iran during 2008-2010 and evaluate its relationship with ethnicity.

**Materials and Methods:** Data was extracted from the nationwide Iranian cancer registry system during 2008-2010. Pathologies and grade was extracted from scanned reports of patients' pathologies by a urologist.

**Results:** The average 3-year age standardized incidence rate of prostate cancer during the study period was 11.52 per 100000 males. The age standardized incidence rates for Persian, Arab, Turkish and Turkmen, Lor, Kurd and Baluch ethnicities were 13.5, 9.3, 7.9, 7.9, 7.2 and 2.1 per 100000, respectively. Poisson regression analysis revealed a statistically significant difference in incidence of prostate cancer in Baluch ethnicity ( $P = 0.028$ ) and a near significant difference for incidence of prostate cancer in Turk-Turkmen and Kurd ethnicity ( $P = 0.067$  and  $P = 0.082$ ) in comparison with Persian ethnicity. The median Gleason score distribution of prostate cancer was not concordant to the age standardized incidence rates. 97% of all pathologies were adenocarcinoma of the prostate followed by malignant carcinoma (1.9%), and transitional cell carcinoma (1.1%).

**Conclusion:** The incidence of Prostate cancer was different between Baluch and Fars ethnicities in Iran. The lowest ASR of PCa was observed in Baluch ethnicity, however the possibility of underreporting due to less access in Baluch ethnicity cannot be ruled out. The Gleason distribution pattern was not concordant to the incidence distribution of Prostate cancer.

**Keywords:** epidemiology; Iran; prostate cancer; Gleason score; incidence

### INTRODUCTION

Prostate cancer (PCa) is the second most common cancer in the world<sup>(1)</sup> and in Iran has been reported as the second most common cancer among men. Epidemiologic studies have revealed that the incidence of PCa is different in different ethnicities and/or races.<sup>(2)</sup> The incidence of PCa is lower in Iran and Asia relative to Europe and the United states.<sup>(3)</sup>

Iran is a large country in the Middle East hosting more than 80/000/000 people. The location of Iran in the past had been pivotal for transfer from east to west as part of the Silk Road. This strategic location had rendered this country a place for conquering in the past. Iran has been occupied by Greeks, Arabs, Mongols and Turks over the past two millennia. As a result, the ethnical distribution of Iran includes Azeri (Turkish and Turkmen) ethnicity in the North West who have close ethnical relationship with Turks of Turkey and central Asia, Arabs in South West who have close ethnical relationship with Arabs of the Persian Gulf, Kurds in West with close ethnical relationship with Kurds of Iraq and Turkey, Baluchs in South East with close ethnical relationship with Baluchs of Pakistan, and Persian ethnicity in North and central parts which constitutes the major predominant ethnicity in Iran (Figure 1).<sup>(4)</sup>

Few reports have previously evaluated the association

of ethnicity with PCa incidence;<sup>(5)</sup> however these comparisons were not flawless due to different quality of reporting systems and modernization between the Middle East and central Asian countries. The comparison of the incidence of PCa in Iran with ethnicity has not been reported before. Neither the nationwide grade of cancer has been reported earlier. In this study, we report the 3-year incidence of PCa and its Gleason score in Iran from 2008-2010 and investigate the relation of this incidence with ethnicity and geography.

### MATERIALS AND METHODS

Data was gathered from the Iranian Cancer Registry regarding all incident cases of PCa from 2008-2010 including data regarding the residence location of patients. Scanned reports of pathologies were investigated by experienced personal and urology residents to extract pathologic specifications of cancers including Gleason score.

The Iranian Cancer Registry is an office in the Ministry of Health and Medical Education and collects all data of pathologic specimens from pathology laboratories, outpatient clinics and treatment centers. Data were checked to remove duplicate cases.

In order to adjust the incidence estimates by age (Age standardized rates or ASRs), we directly standardized

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**Table 1.** Poisson regression comparing the incidence rate of prostate cancer in different ethnic groups (Persian ethnicity was considered as the comparison group)

| Ethnicity    | IRR  | 95% Confidence Interval | P-Value |       |
|--------------|------|-------------------------|---------|-------|
| Kurd         | 0.69 | 0.46                    | 1.05    | 0.082 |
| Turk&Turkmen | 0.72 | 0.51                    | 1.02    | 0.067 |
| Arab         | 0.87 | 0.52                    | 1.44    | 0.584 |
| Lor          | 0.87 | 0.57                    | 1.33    | 0.534 |
| Baluch       | 0.22 | 0.06                    | 0.85    | 0.028 |
| constant     | 9.73 | 8.23                    | 11.50   |       |

the crude incidences of PCa by the standard WHO suggested population. For each province of Iran, we estimated ASR based on its population. The population of each year of each province was estimated based on 2011 and 2006 censuses by geometric method. We estimated the population of each province for each age group of males separately. We used the following equation for population estimation of each year:  $P_t = P_0(1+r)^t$

These estimates provided the denominators necessary for ASR estimates. For each year we estimated ASRs separately then we estimated the weighted average of the three years of 2008-2010 based on the total male population of each year. In order to assess the clustering of prostate incidence in the country, we estimated Moran I index and its related *P* value. We considered *P* values less than 0.05 as statistically significant. The Statistical Package for Social Sciences (SPSS version 25), Excel (2016) and ArcGis (10.2) was used for statistical and spatial analysis of data.

## RESULTS

According the results of the cancer registration data in 3 years of 2008-2010 the average ASR of prostatic cancer in Iran was 11.52 per 100000 males (95% Confidence interval: 11.12-11.93 per 100000 males). **Figure 2** represents the average 3-year ASR of PCa in Iran based on different provinces. Dark colors of map represent higher average 3-year ASRs. As illustrated, the highest ASR is observed in the capital province of Tehran illustrated by dark red. After Tehran, high ASRs are observed in central provinces of the country (mostly of Persian ethnicity) and the lowest ASR is estimated from a province located near Pakistan border which is the Sistan & Baluchestan province hosting Baluch ethnicity. The differences between the ASRs of PCa in different provinces is statistically significant ( $P < 0.05$  corrected for multiple comparisons).

The ethnicity map of Iran including the settlement of different ethnicities (Kurdish, Turkish and Turkmen, Persian, Arabs, and Baluchs) has been depicted in **Figure 1**. The ASR, of PCa in the aforementioned ethnicities in Iran were 13.5 for Persians, 9.3 for Arabs, 7.9 for Turks and Turkmen, 7.9 for Lors, 7.2 for Kurds and 2.1 for Baluchs. (**Figure 3**) Considering the Persian ethnicity which is the major dominant ethnicity in Iran as the reference category, the difference is PCa incidence for the Baluch ethnicity was statistically significant relative to Persian ethnicity ( $P = 0.028$ ) and also a trend to statistically significance was observed between incidence rates of PCa in Turk&Turkmen and Kurd ethnicities relative to the Persian ethnicity (**Table 1**).

Figure 3 represents the median Gleason score of PCa in different provinces. Gleason score was not available in the Iranian Cancer Registry and was manually ex-

tracted from scanned reports of patients' pathologies. Gleason score data was available only for 11% of the total population of patients. Interestingly, the pattern of median Gleason score distribution does not conform to the pattern of PCa incidence.

The pathologies of PCa included: adenocarcinoma 96.6%, malignant carcinoma 1.9 %, transitional cell carcinoma 1.1%, sarcoma 0.1%, lymphoma 0.1%, and other categories 0.2%, based on ICD-O (3rd edition) classification.

The 3-year incidence of PCa based on age groups have been presented in Figure 4. No significant clustering of PCa ASR was detected according to the spatial analysis ( $P$ -value  $> 0.05$ ).

## DISCUSSION

The findings of this study represent a higher incidence of PCa in the capital and more industrialised states in Iran during 2008-2010. Furthermore, the incidence of prostate cancer was higher in Persian ethnicity, moderate in Turkish, Lors, Kurdish, Arab ethnicities, and lowest in Baluchs ( $P$ -value for Baluch versus Persian ethnicity:  $P = 0.028$ ) To our best knowledge, this is the first study to provide the relationship of PCa incidence with ethnicity in the Middle East/Central Asian ethnicities within a single country.

The incidence of PCa has been lower in Asian and African countries in comparison with Europe and the US.<sup>(3)</sup> The ASR of prostate cancer has been reported 174 in 2007 and after a substantial decrease consequent to the recommendation of the United States Preventive Services Task Force against PSA screening was still at 114 in 2012.<sup>(6,7)</sup> The incidence of prostate cancer in Europe was estimated 96 in 2012.<sup>(8)</sup> In the GLOBOCAN report, the lowest worldwide rate of regional prostate cancer ASR was for south-central Asia with an ASR of 4.1 and the highest for Australia/New Zealand with an ASR of 104 in 2008 illustrating wide worldwide differences in PCa incidence.<sup>(9)</sup> In the 2010 GLOBOCAN report, the world ASR of prostate cancer has increased from 27.9 of the 2008 report to 31.1 in 2012.<sup>(8)</sup> Iran has been included in the central-south Asia with an average ASR of 4.5 in the 2012 report consisting the lowest regional reported ASR of PCa in the world. The average regional ASR of PCa for western Asian countries which includes western neighboring countries of Iran (Turkey, Azerbaijan, Armanestan, Iraq, Kuwait, and Saudi Arabia) was 28 in this report highlighting a great regional difference.

A steady increase in the incidence has been reported in many developing countries in the past decades.<sup>(10-12)</sup> Recent studies in the US however present a recent decrease in the incidence of prostate cancer in the past decade after recommendations against PSA screening as described earlier.<sup>(6)</sup>



Figure 1. Ethnic distribution within Iran.

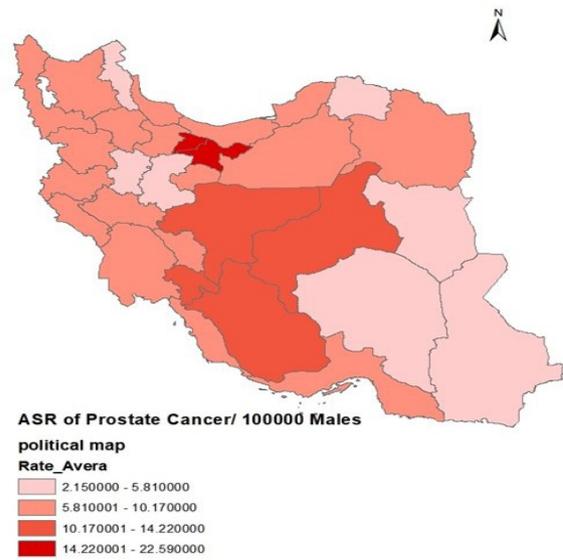


Figure 2. The 3-year average ASR of prostate cancer in different provinces of Iran during 2008 – 2010.

The incidence of PCa in Iran has been constantly increasing: the average ASR of PCa was reported 5.1 during 1996-2000,<sup>(1)</sup> which increased to 5.4 in 2003 and 12.6 in 2009<sup>(12)</sup> which represents more than 100% increase during a decade. The reasons for such a dramatic increase have been attributed to better reporting systems, modernized diet, and lifestyle, and more frequent use of PSA screening.<sup>(12,13)</sup> The Gleason distribution of PCa depicted in Figure 3 favors the theory of better reporting systems as still in less developed provinces with the lowest incidence of PCa, high mean Gleason scores were observed which implies under-reporting or less access to health facilities in these areas. Limited previous publications from Iran have reported

the incidence of PCa in different provinces and all such publications have reported the incidence of PCa in a limited number of provinces or have focused on the age distribution of incident PCa without analyzing the geographical distribution of PCa in Iran. The importance of such investigation lies in ethnic diversities in Iran that as depicted in **Figure 1** which enables the investigation of the influence of ethnicity of PCa incidence adjusted for development and reporting system quality. Moore and colleagues reported the geographical distribution of PCa in central Asia.<sup>(5)</sup> Despite marked observed differences in the incidence of PCa, they concluded that a crude comparison of ASR is not flawless regarding the quality of cancer registries and different levels of mod-

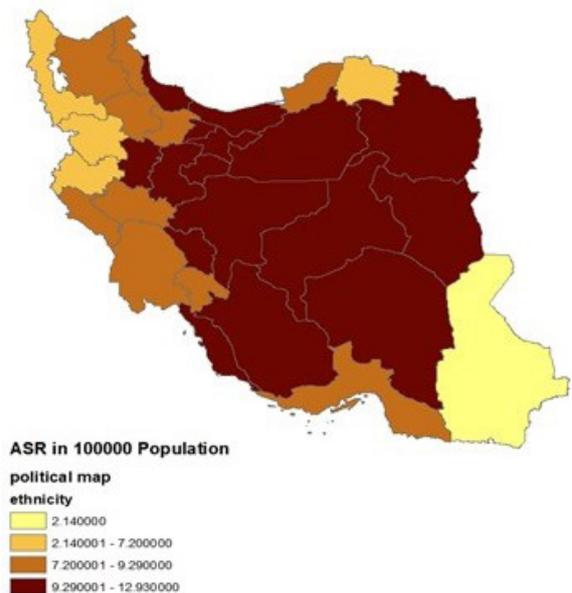


Figure 3. The average 3-year ASR of prostate cancer in different ethnicities within Iran.

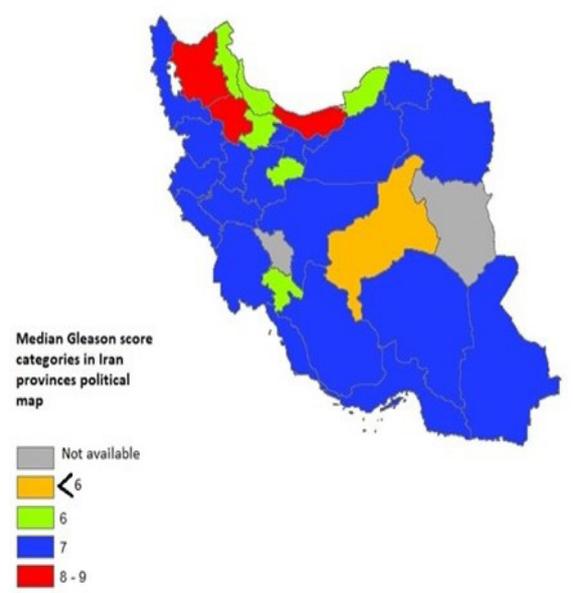


Figure 4. Distribution of prostate cancer Gleason score within Iran.

ernization within these countries. In the current study, we compared ASRs of PCa in different ethnicities within one country with a single cancer registry system and with less diversity in modernization within its states. The lowest observed ASR was in Baluch ethnicity who settle in a southeast province of Iran and have close ethnic origins with Baluchs of Pakistan. This observation becomes interesting when we note that the incidence of kidney and bladder cancer in Baluch ethnicity is one of the lowest ASRs in Iran (Data In press). The ASR incidence of PCa in Pakistan during 1998-2002 was reported 10.1 by Bhurgri et al.<sup>(14)</sup> Nevertheless, one of the reasons which may underlie such an observation can be the access level of different regions to health facilities as people in remote provinces may have less access to health facilities. We could not find studies focusing on the access level of different provinces within Iran to diagnostic and surgical facilities regarding cancer, however, one recent study in Iran aiming to study access inequality in cardiovascular services failed to reveal statistically significant differences in the provision of CCU beds in different regions of Iran<sup>(15)</sup>.

The average 3-year ASR of PCa in decreasing order were observed in Persian ethnicity, then in Arab ethnicity, then in Lor and Turk ethnicity, then in Kord ethnicity, and at last the lowest ASR was observed in Baluch ethnicity respectively. In contrast, the statistics presented by Moore et al. revealed a higher incidence of PCa in Turkey, Azerbaijan, and Armanestan (mainly including Turk&Turkmen ethnicity) relative to Iran.<sup>(5)</sup> The primary objective of this research was to investigate whether there are any differences in PCa incidence across Iranian ethnicities which are located in different geographical locations within Iran. The reason for the observed differences was beyond the scope of the current study. One can attribute the observed differences to differences in geographical climate, dietary patterns, and quality of life within investigated ethnicities. Contemporary studies on quality of life and food security of Iranian provinces during the study period fail to reveal mapping of PCa incidence with quality of life or food security within Iranian provinces.<sup>(16,17)</sup>

The next noticeable observation is the pattern of median Gleason score distribution in this study. To our best knowledge, no prior nationwide study has investigated Gleason score of PCa in Iran. **Figure 3** illustrates that the lowest median Gleason score was observed in Kerman province which is one of the provinces with relatively high ASR of PCa. The political map of Gleason score reveals that the median Gleason score in most Iranian provinces is 7. Isolated provinces with a median Gleason score of 6 include Kohkiluyeh and Boyer-Ahmad, Qom, Golestan, Gilan, and Ardebil. Provinces with a median Gleason score of 8-9 (highest median Gleason score) were Mazandaran, Zanjan, and East Azerbaijan. As indicated previously there is no obvious concordance between ASR of PCa in reported provinces and median Gleason score of cancers in these provinces.

Around 97% of all pathologies were adenocarcinoma of the prostate. This observation has also been reported from other neighboring countries as more than 90% of pathologies in studies from Saudi Arabia and Pakistan were adenocarcinoma.<sup>(18,19)</sup> The trend of adenocarcinoma relative frequency with time was reported negative in Iran (decreasing relative frequency of adenocarcino-

ma type relative to all PCa frequencies each year) by Pakzad et al.<sup>(13)</sup> during 2003-2008. In the current study, a statistically significant decrease was observed from 97.0% in 2008 and 97.6 in 2009 to 95.5% in 2010.

In considering the results of the current study the following limitations should be taken into consideration: The data of the current study is based on the Iranian Cancer Registry System during the years 2008-2010. Any weakness in the Iranian Cancer Registry System including inequality of access to health care across different provinces can affect the results and conclusions of this study. Also, the grade of cancer according to ICD-0 is different from the commonly used Gleason score used in prostate cancer. We manually extracted the Gleason score from scanned copies of patients' pathological reports. However, the number of patients with a total Gleason score report was only 11% of the total patients population.

## CONCLUSIONS

In conclusion, the results of this study reveal a higher incidence of PCa in Iran in modernized provinces in Persian ethnicity and lower in Baluch ethnicity. The median Gleason Score pattern is not concordant with the PCa incidence pattern and in the states with lowest incidences of PCa, a moderate to high median Gleason Score was observed. The most prevalent pathology was adenocarcinoma in 97% of cases. The age distinction pattern is similar to neighboring countries and different from European countries and the US.

## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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