

Clustering 46 Asian countries according to the trend of breast cancer incidence rate from 1990- 2016: An application of growth mixture model

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Abstract

Breast cancer among Asian countries is the second cause of cancer death and remains as a challenging issue in woman health as 39% of all new cases of breast cancer have been diagnosed in Asia. The current study was devoted to recognize different patterns of breast cancer incidence rate among Asian countries. Information about the incidence rates of female breast cancer within 1990-2016 years was extracted from Gapminder web site and growth mixture model was developed to describe the growth patterns and provide a set of tools to investigate the individual differences in change. Our findings suggest an overall increasing trend throughout the continent, but individual trajectories show different behaviors among countries. Bayesian information criterion showed that 3-cluster model was the best. Cluster one countries including: Bangladesh, Israel, Kyrgyz republic, Maldives, Nepal, North Korea, Tajikistan and Timor-Leste, the slope of -0.13 suggests a slight negative trend for the incidence rate of breast cancer. 17 countries including: Armenia, Bahrain, Brunei, Cyprus, Iraq, Japan, Jordan, Kazakhstan, Kuwait, Lebanon, Malaysia, Pakistan, Philippines, Qatar, Singapore, South Korea, United Arab Emirate which belongs to cluster 2, had not only a high intercept that means higher amounts of incidence rate in 1990 year, but also a slope of 0.96, indicating a sharp increase trajectory. Also slope of 0.38 showed a slow increase in the incidence rate of breast cancer over time for another 21 countries. In conclusion, increase of breast cancer incidence among cluster 2 countries is tremendous therefore effective strategies for prevention are urgently needed.

Background

Breast cancer (BF) is known as the most common cancer among women in several countries worldwide [1] [2]. Globally, it includes 23% of all cases of cancers and 14% of the cause of cancer death in women [3]. According to the 2012 GLOBOCAN, the incidence of age standardized BF is 73.4 per 100000 in developed countries and 31.3 per 100000 in developing countries [4].

44% of deaths and 39% of all new cases of breast cancer have been diagnosed in Asia. Approximately, 25% of women's cancer in India is breast cancer [5]. Breast cancer among Asian countries is the second cause of cancer death and remains as a challenging issue in woman health [6]. In Arab countries like Qatar, Saudi Arabia, Iraq and Bahrain, breast cancer is a crucial issue [7]. In Saudi Arabia, the International Research Agency announced that the incidence rate of breast cancer in 2009 was 22.4 per 100000 in women and mortality rate was 10.4 per 100000 [8]. BC is also the most common cancer in China and the fifth cause of women's death due to cancer [9] as in 2015, 268,600 new cases and 69,500 deaths because of breast cancer were reported in China [10].

Although the trend of breast cancer incidence across most of the Asian countries is increasing, heterogeneity among countries is particularly apparent due to different health policies, regional behaviors, and genetic and lifestyle variety [6]. While the incidence rate of breast cancer has doubled or more in Korea, Singapore, Hong Kong and Japan, besides socioeconomic advancement [10] in the last decades

[6, 11], a substantial increase was found in China (2.96% per year) [12], Thailand [13] and Taiwan [3]; also, a gradual increase was reported in Sri Lanka [14], Pakistan [15], India [16], and Iraq [17].

Growth mixture modeling as one of the well-known and practical statistical methods is capable of dividing a heterogeneous population into multiple homogeneous clusters based on their temporal trends (detecting, growth mixture). To the best of our knowledge, there are a few studies about diversity of temporal trends of breast cancer in Asia, and previous studies are limited to a country or regional location. Therefore, the current study was devoted to cluster most of the Asian countries according to the trend of breast cancer incidence rate for the 27-year period (1990–2016) via growth mixture models to show longitudinal heterogeneity among the countries.

Methods

In the current study, information about the incidence rates of female breast cancer (new cases per 100,000 women) within 1990–2016 years was extracted from Gapminder web site for 46 Asian countries. Gapminder is a non-profit venture registered in Stockholm, Sweden and the current dataset provided by the World Health Organization in Gapminder.

Growth mixture model (GMM) was developed to describe the growth patterns and provide a set of tools to investigate the individual differences in change. GMM tries to explore latent profiles of temporal trends by incorporating the mixed models to consider the intra- correlation of individuals in repeated measures. This method also identifies and discriminates heterogeneous unobservable clusters called latent groups using the latent models (Growth mixture model, GMM paper). In GMM, estimating the optimal number of latent classes is a critical issue. In the current manuscript, Bayesian information criterion (BIC) was used to estimate the optimum number of latent clusters; all the statistical analyses were performed in Mplus software, version 7.4.

Results

Visualized trend of breast cancer incidence rate among 46 Asian countries is shown in Figure 1 and related descriptive statistics in 5-year intervals from 1990 to 2016 are reported in Table 1. Reported results suggest an overall increasing trend throughout the continent, but individual trajectories show different behaviors among countries. To consider heterogeneity in growth trajectories and model these complex patterns, we implemented the growth mixture model.

Bayesian information criterion (BIC) showed that 3-cluster model was the best model with minimum error (results not shown). Therefore, growth trajectories for 3-cluster model were fitted and for each cluster, intercept and slope of the incidence rate were obtained. As shown in Table 2, eight countries belonged to cluster 1, seventeen countries to cluster 2, and the other 21 countries belonged to cluster 3.

The entropy was another goodness of fit index which was in an acceptable level (entropy=0.96). Figure 2 shows both overall mean trends and estimated linear trajectories for different clusters.

Estimated slopes help us to find more information about the growth of breast cancer in the last decades among Asian countries. For cluster one countries (including: Bangladesh, Israel, Kyrgyz republic, Maldives, Nepal, North Korea, Tajikistan and Timor-Leste), the slope of -0.13 suggests a slight negative trend for the incidence rate of breast cancer; incidence rate is almost constant over time. 21 countries in cluster 3 (including: Afghanistan, Azerbaijan, Bhutan, Cambodia, China, India, Indonesia, Iran, Lao, Mongolia, Myanmar, Oman, Palestine, Saudi Arabia, Sri Lanka, Syria, Thailand, Turkmenistan, Uzbekistan, Vietnam and Yemen) showed a slow increase in the incidence rate over time. 17 countries (including: Armenia, Bahrain, Brunei, Cyprus, Iraq, Japan, Jordan, Kazakhstan, Kuwait, Lebanon, Malaysia, Pakistan, Philippines, Qatar, Singapore, South Korea, United Arab Emirate) which belongs to cluster 2, had not only a high intercept that means higher amounts of incidence rate, but also a slope of 0.96, indicating a sharp increase trajectory (Table 2 and Figure 2).

Discussion

In our study on 46 Asian countries, three types of behavior were noticed. The first cluster consists of the countries with a slight negative trend for incidence rate of breast cancer incidence rate: Bangladesh, Israel, Kyrgyz republic, Maldives, Nepal, North Korea, Tajikistan and Timor-Leste. The second one is the cluster with sharp increase trajectory: Armenia, Bahrain, Brunei, Cyprus, Iraq, Japan, Jordan, Kazakhstan, Kuwait, Lebanon, Malaysia, Pakistan, Philippines, Qatar, Singapore, South Korea, United Arab Emirate. The last group is the one with slow increase in incidence rate: Afghanistan, Azerbaijan, Bhutan, Cambodia, China, India, Indonesia, Iran, Lao, Mongolia, Myanmar, Oman, Palestine, Saudi Arabia, Sri Lanka, Syria, Thailand, Turkmenistan, Uzbekistan, Vietnam and Yemen.

Previous studies done in eastern and southeastern Asia from 1993 to 2002 showed that all of the countries experienced an increase in breast cancer rate from the first 5 year period to the second. Although the rates are different in various countries, Korea and Thailand had the highest (44.9% and 36.0%) and Philippines had the lowest (5.2%) incidence rates. Korea had the significantly increased incidence rates during the 10 year period. Four patterns in the incidence rates and age specific incidence in the study of Shin et al. were suggested. Low incidence with slow increase until age 50 years and then a gradual decrease were seen in rural China, Korea and Thailand. Intermediate incidence with increase until age 50 years and then slow decrease in the elderly is the second pattern in Japan and Taiwan. Hong Kong and Shanghai showed an intermediate incidence with rapid increase until age 50 years and then a plateau. The last pattern is high incidence with rapid increase peaking after age 65 in Singapore and Philippines. This study claim that early age at menarche and late in menopause, delay in marriage, fewer children, changes in infant feeding, and lifestyle are the risk factors of breast cancer [18]. Based on a study conducted in Turkish Republic of North Cyprus that was done from 2007 to 2012, similar to our results, it was reported that the trend of BC incidence rate in Asian was rising. Hormonal therapy, fewer children, late menopause, early menarche, late reproductive and obesity are considered to be the risk factor of breast cancer [19].

Study of Poudel et al. in Nepal illustrated the breast cancer as the second most common cancer of women over the period of 2003 to 2012 years. In contrast to our findings, the incidence rate rose from 2.35 in 2003 to 4.59 in 2012. This rise may be due to lack of information on breast cancer risk factors and breast screening [20]. The difference between the obtained results may be due to different periods of time. Also, previous studies about breast cancer incidence during 1993 to 2012 years showed that North Korea had a slight decrease and South Korea had a sharp increasing trend that was consistent with obtained results in the current study [18].

A study in Pakistan claimed that total projected breast cancer incidence will increase by approximately 23.1% in 2020 to 60.7% in 2025 and cases of breast cancer diagnosed in younger women aged 30 to 34 years will increase from 70.7 to 130.4% in 2020 and 2025 as compared to 2015. From 2004 to 2015, breast cancer rates were lower and stable in the age of 15 to 29 years, while the incidence rates for women aged 25 years and older were increasing overall with a slight variation. In 2004 to 2015, the incidence rates were the highest among those aged 60 to 64 years. However, from 2016 to 2025 increases in breast cancer rates among women aged 55 to 64 years and older than 75 years were expected. Lifestyle factors like smoking, physical activity, westernized diet, illiteracy, and cultural and economic status are the influencing factors [21].

In line with our study, previous studies in Lebanon confirmed a high increase in breast cancer incidence. Lakkis et al. showed that age standardized rate of BC in Lebanon was 46.7 per 100000 in 1998 which increased to 52.5 in 2002. This increase is higher than several Asian countries like Iran, Malaysia and Japan. The reasons of increase may be related to improvement of NCR data collection and the rise in the use of mammography. Reproductive factors such as mean age at marriage of the women increased from 23.2 in 1970 to 27.5 in 1996, and also the fertility rate decrease from 4.4 to 2.5 during the same period. The age of menarche and menopause became younger and later, respectively. Hormone replacement therapy and obesity, smoking and nargileh use among Lebanese women were the other possible risk factors [22].

In a study done in Singapore, the overall incidence rate of breast cancer was totally increased from 1968 to 2002. The aforementioned increase was 3.1% per year for the Chinese, 2.8% per year for Malaysians and 1.7% per year for Indians who were living in Singapore. Singapore's transition from an industrialized country to a developed country has brought about changes in lifestyle in the population: late marriage, delay in child bearing, smaller family sizes, and genetic interaction are the reason of the change in the breast cancer incidence in Singapore. Other risk factors like reproductive issues, height, dietary habits, obesity, duration of breast feeding, childhood growth, age at menarche and menopause make variations in different ethnic groups and could also influence breast cancer risks [23].

A cross-sectional study in Kazakhstan reported that 45891 cases of breast cancer were registered during 1999 to 2013, and 20112 women died of this. These figures showed an increase in the incidence and a decrease in mortality. Astana and Almaty showed a high incidence rate in Kazakhstan. Ethnicity and compliance with screening recommendation affect breast cancer [24].

Zahmatkesh et al. showed that the trend of breast cancer incidence in 2000–2002 in Iran had a steep increasing slope due to the evolution of Iranian cancer registration system [25]; similar to our study, from 2005–2009 the trend had a mild slope. However, another study among Iranian women showed a considerable increase from 15.96 per 100000 in 2003 to 33.21 per 100000 in 2008, which is not consistent with our study. This may be due to difference in the speed of lifestyle changes and exposure to risk factors in various provinces like lack of physical activity, pattern of reproduction and obesity [26].

A study in India showed that the age standardized incidence rates of breast cancer increased from 24.8 in 1988 to 41.0 in 2012 in Delhi. Also, they claimed that a statistically significant increase in breast cancer was also seen in Delhi over 25 years. The same pattern was also reported among Indian urban registries. This trend has occurred due to adherence to more westernized lifestyle like adverse changes in diet, physical activity, and fertility and reproductive pattern [16].

Our findings showed a slow increase in the incidence rate of breast cancer in China that was approved in previous studies. For example, the study of Yang et al. showed that the incidence rate of female breast cancer in urban areas of Beijing was 55.43 in 2004 and rose to 70.7 per 100000 women in 2008. Besides, in rural areas it was 30.6, which increased to 44.78 per 100000 women in 2008 [27].

Breast cancer incidence rate in China in 2015 had a sharpe increase from 1.17 per 100000 women aged 20 to 24 years to 12.75 per 100000 women aged 65 to 69 years. In India, the breast cancer incidence rate was 77.28 per 100000 women aged 50 to 54 years and 78.15 per 100000 women in 70 to 74 years and 86.33 per 100000 women in 2015. Also, in Thailand an increasing trend was seen in 20_24 to 45_49 year old women and then decreased. The reasons of the aforementioned trends in these countries are socio-cultural background, poverty, increasing population and limited access to advanced screening diagnosis and treatment [28].

Crude incidence of BC in Saudi Arabia was 6.8 per 100000 women in 2001 and 11.4 per 100000 women in 2006. This rate was 14.3 per 100000 women in 2007 and then it dropped by 1.4 points in 2008. The highest increase was reported in Jouf from 2001 to 2008. Qassim, Jazan and Tabuk revealed a decreasing rate and the lowest changes with down trending in this. In other study in Arab world a gradually increasing incidence was seen from 1990 to 2016, like the global trend. This trend in Arab world will increase over the next 10 years. Incidence of breast cancer was 28 per 100000 women in 2016. Lebanon, Bahrain and morocco had the highest incidence rate among Arab nations, respectively [8].

Taiwan had an increasing trend from 1970 to 2000 (6.23 to 23.76 per 100000). In 1996, there were 3801 cases in South Korea (16.7 per 100000) and it increased to 9668 in 2004 (40.5 per 100000)[29].

Srilanka showed the increasing age standardized incidence of breast cancer from 9.2 in 2001 to 12.9 per 100000 in 2010. However, a slight drop in the incidence was observed in 2007. These trends are related to westernization of lifestyle such as the use of unhealthy food, inactive life that causes obesity, delay in childbearing, and duration of breastfeeding [14].

Changes in demographic and the risk profile of population are related to the increasing trend of BC in Thailand. In two surveys in 2004 and 2009, the percentage of overweight, diabetes or hypertension was found to be increasing. The rate of parity and total fertility was 6 in 1970, 3 in 1985, 2 in 1998, and 1.6 in 2020 [13].

Conclusion

In conclusion, increase of breast cancer incidence among cluster 2 countries is tremendous therefore effective strategies for prevention are urgently needed.

Declarations

Ethics approval and consent to participate: not applicable

Consent for publication: not applicable

Availability of data and materials: data are available at Gapminder web site.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: FA analyzed the data, write the manuscript and approved final version. KM analyzed the data, write the manuscript and approved final version. HR analyzed the data, write the manuscript and approved final version.

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References

1. Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA: **Global trends in breast cancer incidence and mortality 1973–1997**. *International journal of epidemiology* 2005, **34**(2):405-412.
2. DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO, Jemal A: **International variation in female breast cancer incidence and mortality rates**. *Cancer Epidemiology and Prevention Biomarkers* 2015, **24**(10):1495-1506.
3. Chang H-T, Shi H-Y, Wang B-W, Yeh S-CJ: **Breast cancer incidence and predictors of surgical outcome: a nationwide longitudinal study in Taiwan**. *Clinical Oncology* 2017, **29**(6):362-369.
4. Wen D, He Y, Wei L, Zhang N, Li S, Wen X, Yang Y, Wang G, Wang S, Geng C: **Incidence rate of female breast cancer in urban Shijiazhuang in 2012 and modifiable risk factors**. *Thoracic cancer* 2016, **7**(5):522-529.

5. Madhav MR, Nayagam SG, Biyani K, Pandey V, Kamal DG, Sabarimurugan S, Ramesh N, Gothandam KM, Jayaraj R: **Epidemiologic analysis of breast cancer incidence, prevalence, and mortality in India: Protocol for a systematic review and meta-analyses.** *Medicine* 2018, **97**(52).
6. Ghoncheh M, Mahdavifar N, Darvishi E, Salehiniya H: **Epidemiology, incidence and mortality of breast cancer in Asia.** *Asian Pacific journal of cancer prevention* 2016, **17**(S3):47-52.
7. Ahmadi A, Ramazani R, Rezagholi T, Yavari P: **Incidence pattern and spatial analysis of breast cancer in Iranian women: Geographical Information System applications.** *Eastern Mediterranean Health Journal* 2018, **24**(4):360-367.
8. Alghamdi IG, Hussain II, Alghamdi MS, El-Sheemy MA: **The incidence rate of female breast cancer in Saudi Arabia: an observational descriptive epidemiological analysis of data from Saudi Cancer Registry 2001–2008.** *Breast Cancer: Targets and Therapy* 2013, **5**:103.
9. Zhou H-B, Liu S-Y, Lei L, Chen Z-W, Peng J, Yang Y-Z, Liu X-L: **Spatio-temporal analysis of female breast cancer incidence in Shenzhen, 2007–2012.** *Chinese journal of cancer* 2015, **34**(3):13.
10. Cheng Y, Yan Y, Gong J, Yang N, Nie S: **Trends in incidence and mortality of female breast cancer during transition in Central China.** *Cancer management and research* 2018, **10**:6247.
11. Shin HR, Boniol M, Joubert C, Hery C, Haukka J, Autier P, Nishino Y, Sobue T, Chen CJ, You SL: **Secular trends in breast cancer mortality in five East Asian populations: Hong Kong, Japan, Korea, Singapore and Taiwan.** *Cancer science* 2010, **101**(5):1241-1246.
12. Huang Z, Wen W, Zheng Y, Gao Y, Wu C, Bao P, Wang C, Gu K, Peng P, Gong Y: **Breast cancer incidence and mortality: trends over 40 years among women in Shanghai, China.** *Annals of Oncology* 2016, **27**(6):1129-1134.
13. Sangkittipaiboon S, Leklob A, Sriplung H, Bilheem S: **Breast cancer in Lopburi, a province in central Thailand: Analysis of 2001–2010 incidence and future trends.** *Asian Pac J Cancer Prev* 2015, **16**:8359-8364.
14. Fernando A, Jayarajah U, Prabashani S, Fernando EA, Seneviratne SA: **Incidence trends and patterns of breast cancer in Sri Lanka: an analysis of the national cancer database.** *BMC cancer* 2018, **18**(1):482.
15. Soomro R: **Is breast cancer awareness campaign effective in Pakistan?** *Perspective* 2017, **67**(7).
16. Manoharan N, Nair O, Shukla N, Rath GK: **Descriptive Epidemiology of Female Breast Cancer in Delhi, India.** *Asian Pacific journal of cancer prevention: APJCP* 2017, **18**(4):1015.
17. Habib OS, Hameed LA, Ajeel NA, Al-Hawaz MH, Al-Faddagh ZA, Nasr GN, Al-Sodani AH, Khalaf AA, Hasson HM, Abdul-Samad AA: **Epidemiology of breast cancer among females in basrah.** *Asian Pac J Cancer Prev* 2016, **17**:91-95.
18. Shin H-R, Joubert C, Boniol M, Hery C, Ahn SH, Won Y-J, Nishino Y, Sobue T, Chen C-J, You S-L: **Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women.** *Cancer Causes & Control* 2010, **21**(11):1777-1785.
19. Pervaiz R, Tulay P, Faisal F, Serakinci N: **Incidence of cancer in the Turkish Republic of Northern Cyprus.** *Turkish journal of medical sciences* 2017, **47**(2):523-530.

20. Poudel KK, Huang Z, Neupane PR: **Trend of cancer incidence in Nepal from 2003 to 2012.** *Asian Pac J Cancer Prev* 2016, **17**(4):2171-2175.
21. Zaheer S, Shah N, Maqbool SA, Soomro NM: **Estimates of past and future time trends in age-specific breast cancer incidence among women in Karachi, Pakistan: 2004–2025.** *BMC public health* 2019, **19**(1):1001.
22. Lakkis NA, Adib SM, Osman MH, Musharafieh UM, Hamadeh GN: **Breast cancer in Lebanon: incidence and comparison to regional and Western countries.** *Cancer epidemiology* 2010, **34**(3):221-225.
23. Sim X, Ali RA, Wedren S, Goh DL-M, Tan C-S, Reilly M, Hall P, Chia K-S: **Ethnic differences in the time trend of female breast cancer incidence: Singapore, 1968–2002.** *BMC cancer* 2006, **6**(1):261.
24. Beysebeyev E, Bilyalova Z, Kozhakeeva L, Baissalbayeva A, Abiltayeva A: **Spatial and temporal epidemiological assessment of breast cancer incidence and mortality in Kazakhstan, 1999-2013.** *Asian Pac J Cancer Prev* 2015, **16**(15):6795.
25. Zahmatkesh B, Keramat A, Alavi N, Khosravi A, Kousha A, Motlagh AG, Darman M, Partovipour E, Chaman R: **Breast cancer trend in Iran from 2000 to 2009 and prediction till 2020 using a trend analysis method.** *Asian Pac J Cancer Prev* 2016, **17**(3):1493-1498.
26. Rafiemanesh H, Salehiniya H, Lotfi Z: **Breast cancer in Iranian woman: Incidence by age group, morphology and trends.** *Asian Pacific journal of cancer prevention* 2016, **17**(3):1393-1397.
27. Yang L, Sun T, Wang N: **The incidence and mortality trends of female breast cancer in Beijing, China: between 2004 and 2008.** *Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]* 2012, **46**(11):1009-1014.
28. Mubarik S, Malik SS, Wang Z, Li C, Fawad M, Yu C: **Recent insights into breast cancer incidence trends among four Asian countries using age-period-cohort model.** *Cancer Management and Research* 2019, **11**:8145.
29. Leong SP, Shen Z-Z, Liu T-J, Agarwal G, Tajima T, Paik N-S, Sandelin K, Derossis A, Cody H, Foulkes WD: **Is breast cancer the same disease in Asian and Western countries?** *World journal of surgery* 2010, **34**(10):2308-2324.

Tables

Table 1, descriptive statistics of breast cancer incidence rates (per 100000) among 46 Asian countries

Year	Min	Max	Mean	SD	Median
1990	9.6	81.4	25.5	14.7	23.2
1995	10.5	91.8	28.9	16.9	24.6
2000	11.9	90.2	31.8	18.5	25.0
2005	12.5	94.4	35.0	21.1	26.7
2010	12.7	98.8	36.6	21.7	29.6
2016	13.1	99.3	38.7	21.7	33.3

Table 2. Results of 3-cluster model to describe growth patterns of breast cancer incidence rates among Asian countries

Cluster	Number of countries	Intercept		Slope	
		Estimate	SE	Estimate	SE
1	8	18.62	2.48	-0.13	0.06
2	17	37.15	4.44	0.96	0.21
3	21	17.51	4.68	0.38	0.09

Figures

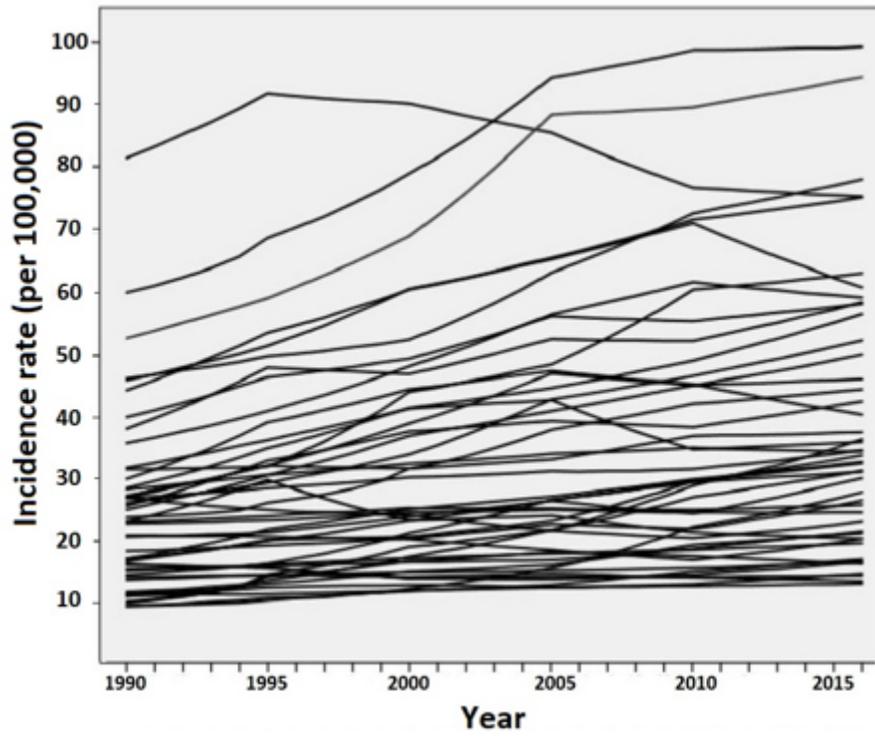


Figure 1

The trend of breast cancer incidence rate among 46 Asian countries

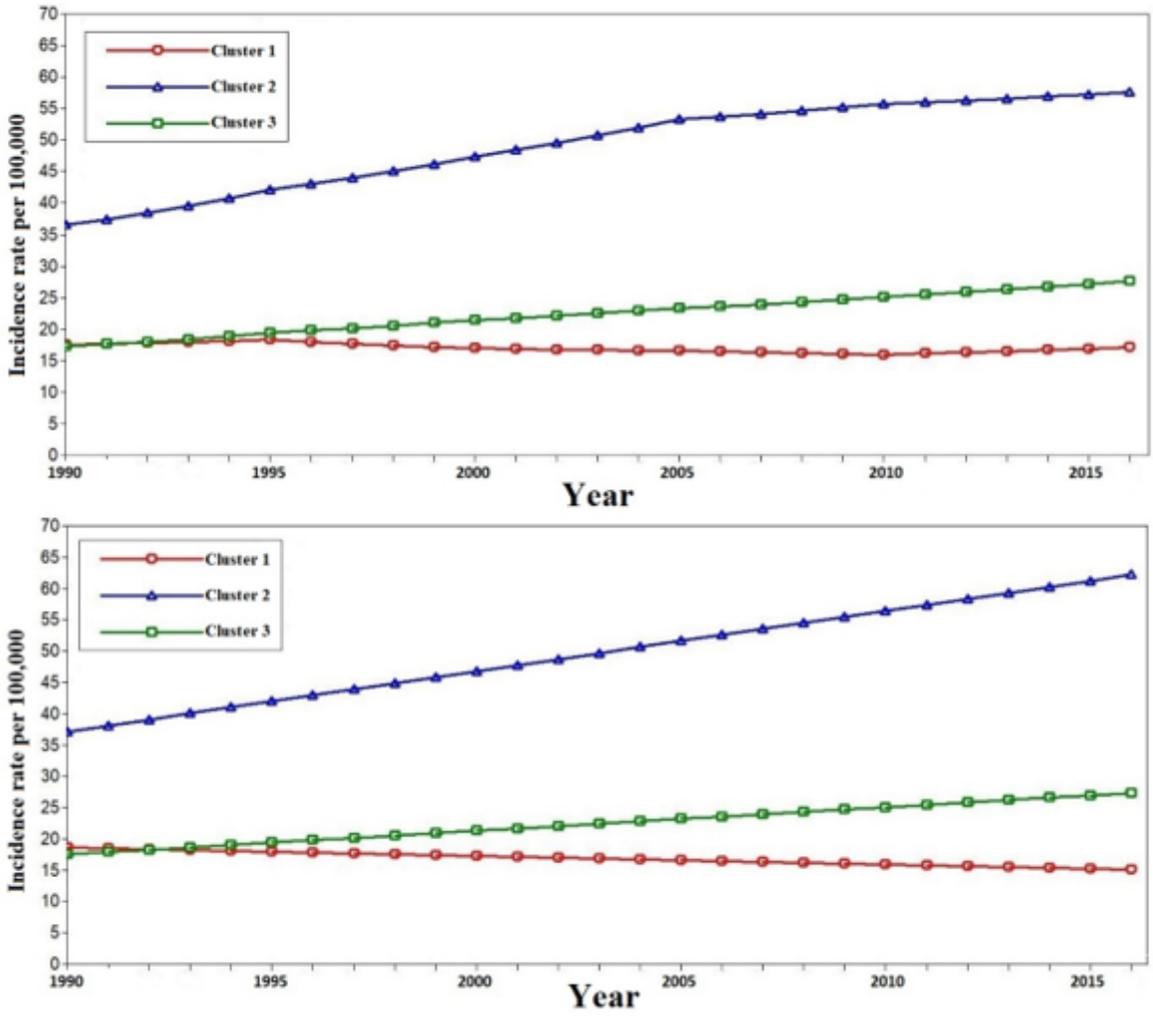


Figure 2

trend of marginal mean and estimated linear trend in different clusters