RESEARCH ARTICLE

Effect of Screening on Variation in Cervical Cancer Survival by Socioeconomic Determinants - a Study from Rural South India

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Abstract

Background: Socioeconomic factors are associated with screening in terms of reducing the risk of cervical cancer. This study aimed to clearly establish the effect of screening on variation in socio-economic factor-specific survival estimates. Materials and Methods: Survival estimates were calculated using the life table method for 165 women from the routine care control arm and 67 from the visual inspection with acetic acid screening arm diagnosed with cervical cancer during 2000-2006 in rural south India. Kaplan-Meier survival curves were plotted to compare the variation in survival by socioeconomic factors. Results: Whereas there was a significant variation in survival estimates of the different categories of age at diagnosis among the screen-detected cancers with women aged<50 years having an improved survival, no significant variation was noted among women diagnosed with cervical cancer from the control arm. Compared to the variation among the cancer cases detected in the unscreened control group, screening widened the variation in survival estimates by age and type of house, and reduced the variation by education. The direction of the magnitude of the survival estimates was reversed within the different categories of occupation, marital status and household income in the screen-detected cancer cases compared to control group cancer cases. Also, women diagnosed with stage 1 disease had a very good survival. Conclusions: Screening changed the pattern of survival by socio-economic factors. We found improved survival rates in screened women aged <50 years, with no formal education, manual workers and married women.

Keywords: Uterine cervical neoplasms - survival rate - rural population - socio-economic determinants - India

Asian Pac J Cancer Prev, **16 (13)**, 5237-5242

Introduction

The capability of health services to provide early diagnosis, treatment and clinical follow-up improves cancer survival (Sankaranarayanan et al., 2010). The goal of cervical cancer screening is to reduce the burden of cervical cancer in a population and the two valid indicators to measure the effectiveness of a screening programme are the reduction in incidence of and mortality from cervical cancer (Sankila et al., 2000). Improvement in survival is a necessary, but not sufficient indicator to measure the beneficial effect of screening because of lead-time, length and over-diagnosis biases (Sankila et al., 2000).

There is large variation in cancer survival between and within countries and it is generally due to the differences in medical, biological, cultural, genetic, geographic and socio-economic factors (Coker et al., 2006; Sankaranarayanan et al., 2010; Global Cancer Facts and Figures, 2012). Socio-economic factors are associated with a person's general health, nutritional status, attitudes, beliefs and health behavior, and it can influence the chances of being detected early, access to or completion of treatment and follow-up, hence determining survival (Sankaranarayanan et al., 1995). The role of socio-economic factors in cervical cancer survival has not been clearly established in many of the survival studies done in India and abroad mainly because the studies were done within a group of patients with similar socio-economic characteristics and/or similar accessibility or inaccessibility to cervical cancer screening, diagnosis and treatment facilities (Schrijvers.,1994; Nandakumar et al., 1995; Coker et al., 2006; Munagala et al ., 2010).

In our previous study it was shown that young, currently married, uneducated and poor women benefitted most from screening in terms of reducing the risk of developing cervical cancer (Thulaseedharan et al ., 2013).

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As a result the authors found it interesting to study who benefitted most from cervical cancer screening in terms of improving survival. Little was found on such studies in the literature. In this paper we describe how screening affected cervical cancer survival according to socio-economic factors. For this study we used the data of 165women diagnosed with cervical cancer from a cohort of 31,000 women in the routine care control arm and 67 women with screen-detected cervical cancer from a cohort of 31,343 women from the intervention arm of a large visual inspection with acetic acid (VIA) screening trial conducted in south India during 2000-2006 (Sankaranarayanan et al., 2007a), and followed until 2012 December.

Materials and Methods

The details of the screening trial were explained in earlier papers (Sankaranarayanan et al., 2003; Sankaranarayanan et al., 2007a; 2007b). Baseline survey and screening were performed in the intervention arm during 2000-2003. The women in the control arm were also surveyed during the same period and the health workers educated the women about screening, symptoms and risk factors of cervical cancer, informed them of the facilities available in the area and advised them to utilize those health care facilities. Health workers carefully explained the study to all participants in both arms and if they agreed to participate, obtained a signed informed consent form in the presence of a witness.

Eligible women aged between 30-59 years from both arms were followed-up in three consecutive years to collect information on death, migration and cervical cancers until December 2006. Also, the study population was matched with the Dindigul Ambillikai Cancer Registry (DACR) database to obtain all incident cervical cancer diagnosed from the study population during 2000-2006 (Sankaranarayanan et al., 2007a). The current study included the data of 165 women diagnosed with cervical cancer during 2000-2006 from the control arm, excluding two women identified only with their death certificates, and another 67 women with screen-detected cervical cancer during 2000 to 2005 from the intervention arm. Overall, 73% (121/165) of the women identified with cervical cancer from control arm and 91% (61/67) of the screen-detected women were diagnosed during 2000-2003, and the remaining women were diagnosed with cervical cancer during 2004-2006. A follow-up survey of the base population was again conducted during 2011-2012 to collect information on death, migration and cervical cancer. For this survival analysis the follow-up information of the women diagnosed with cervical cancer both from the control arm and screen-detected women were obtained from the DACR records in addition to the follow up survey of the base population in 2011-2012.

Variables under study

The factors studied were age at diagnosis (categorized in 30-39, 40-49 and 50+), stage of disease (Stage I, stage II or worse and unknown) and the baseline information on individual and household level socio-economic factors such as: formal education (no or some schooling); occupation (housewife/others and manual workers); marital status (currently married and widowed/separated); Type of house (Thatched and tiled/concrete); and household monthly income (categorized in <INR2000 and >INR2000).

Statistical analysis

The statistical analysis was performed in Stata/IC 11.2 software package (STATA corp, Texas). Follow-up time was calculated by taking date of diagnosis as starting date. The cutoff dates were 2011 December 31st for the women with cervical cancer from the control arm and 2010 December 31st for the screen-detected women. The earlier cutoff date for the screen-detected women was taken because the screening arm had their follow-up survey in 2011. The follow-up status was defined as complete if death had occurred within the cutoff period or the subject had a follow-up after the cutoff with the information that the subject was alive at cutoff date. Among women from control arm, three deaths occurred after cutoff who were considered as alive with a complete follow-up in 2011 December. Similarly, among screen-detected women two deaths occurred after cutoff who were considered as alive with a complete follow-up in 2010 December. Follow-up status was defined as incomplete if the vital status of the women was not known at cutoff. We identified only two subjects out of 165 and one subject out of 67 with incomplete follow-up status due to loss to follow-up. The follow-up time was calculated in years by taking the duration between date of diagnosis and date of death for those who died; 31st December 2011 for those who were alive and had a complete follow-up if cancer diagnosed from control arm; 31st December 2010 for those who were alive and had a complete follow-up if screen-detected cancer; and the date of last seen as alive for those who had an incomplete follow-up status. The survival rates were estimated by life table method and the log rank test was used to test the equality of survivor functions. Kaplan–Meier survival curves were plotted to study whether survival according to socio-economic factors was affected differently by screening.

Results

Table 1 describes the characteristics of 165women identified with cervical cancer from the control arm and 67 women with screen-detected cancer. Compared to screen-detected women the proportion of older women was high among women from control arm (45.5% *vs* 36%). Proportion of stage 1 cancers was 10.9% in women from control arm and 31% in the screen-detected. According to the baseline information 10.3% of women from control arm and 22.4% of screen-detected women were formally educated. The proportion of manual workers was more or less same (63.6% *vs* 61%) in both groups of women. Proportions of currently married women were 88.5% and 79%, and proportions of women lived in tiled/concrete houses were 83.6% and 61% in women diagnosed with cancer from control arm and screen-detected women, respectively. About 71% of women from the control arm reported having a monthly household income less than

2000 INR versus 79% of screen-detected women.

Table 1 also describes the variation in five-year survival according to different characteristics of women in both groups. In order to clearly explain how screening affected the variation in survival by socio-economic factors we illustrated Kaplan Meier survival curves for factors such as: age, education and income. Figure 1 shows that the survival pattern of older women was not changed by screening. Furthermore the survival difference between younger and older women was minimal among women from control arm, but there was a 40% unit difference between the survival of younger and older women if cancer was detected by screening. Women without formal education had an improved survival and it reduced the variation in survival between the educated and uneducated women when cancer was detected by screening (Figure 2). Between the invasive cancer case groups, the survival estimates were similar for women with household income below 2000 INR in the control and screen-detected groups. However, for women with higher incomes (2000+ INR), the survival estimates in the screen-detected group were much higher than their counterparts in the control group

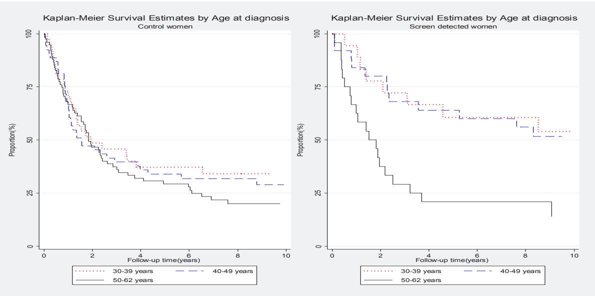

Figure 1. Screening Increased the Variation in Survival by Age at Diagnosis

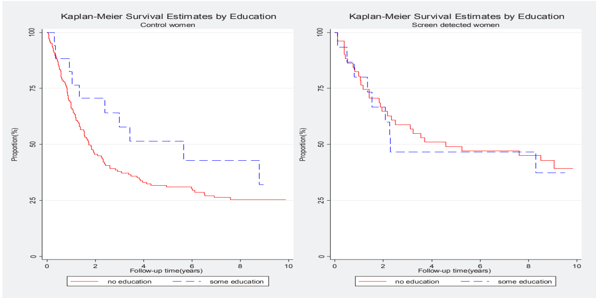

Figure 2. Screening Reduced the Variation in Survival by Formal Education

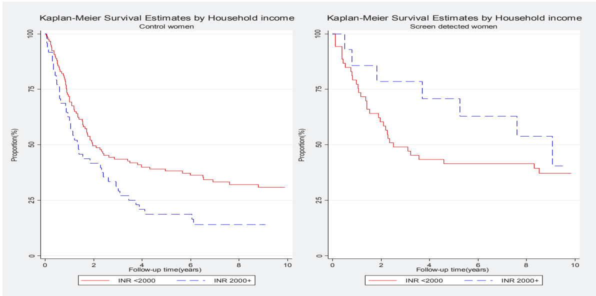

Figure 3. Screening Reversed the Variation in Survival by Household Income

Table 1. Five-year Observed Survival for Women Diagnosed with Cervical Cancer in the Control and Screened Arms

Socio-economic factors	Control arm n	(%)	5-year survival (%)	p-value	Screened arm n	(%)	5-year survival (%)	p value
Cancer cases	165		32.5		67		47.6	
Individual								
Age at diagnosis								
30-39	37	(22.4)	37.3		18	(26.9)	60.4	
40-49	53	(32.1)	34.0		25	(37.3)	60.0	
50+	75	(45.5)	29.1	0.546	24	(35.8)	20.8	0.001*
Stage of disease								
stage 1	18	(10.9)	77.6		21	(31.3)	75.9	
stage2+	105	(63.6)	23.5		45	(67.2)	33.3	0.002*
unknown	42	(25.5)	35.7	0.006*	1	(1.5)		
Education[a]								
No schooling	145	(87.9)	30.9		51	(76.1)	49.0	
Some schooling	17	(10.3)	51.6	0.179	15	(22.4)	46.7	0.821
Occupation								
House wife/others	60	(36.4)	36.4		26	(38.8)	38.4	
Manual	105	(63.6)	30.3	0.312	41	(61.2)	53.6	0.568
Marital status								
Currently married	146	(88.5)	31.3		53	(79.1)	52.7	
Widowed/separated	19	(11.5)	42.1	0.467	14	(20.9)	28.6	0.020*
Household								
Type of house								
Thatched	27	(16.4)	25.9		26	(38.8)	38.1	
Tiled/concrete	138	(83.6)	33.8	0.259	41	(61.2)	53.7	0.233
Income								
<2000	117	(70.9)	38.2		53	(79.1)	41.5	
2000+	48	(29.1)	18.8	0.014*	14	(20.9)	71.1	0.278

[a]The information on education is missing for 3 observations among women from control and one observation among screen-detected women; * Significant at 0.05 level of significance

Table 2. Characteristics of Women Diagnosed with Cervical Cancer Stratified by Age at Diagnosis

	Control Age at diagnosis			Screen-detected Age at diagnosis		
Proportion of women	30-39 (n=37)	40-49 (n=53)	50-62 (n=75)	30-39 (n=18)	40-49 (n=25)	50-60 (n=24)
no education	83.3	86.5	94.6	66.7	72.0	91.3
manual workers	64.9	67.9	60.9	66.7	72.0	45.8
currently married	97.3	94.3	80.0	88.9	88.0	62.5
lived in thatched houses	18.9	11.3	18.7	44.4	36.0	37.5
income ≥2000INR	21.6	34.0	29.3	22.2	24.0	16.7
stage1 cancer	8.1	11.3	12.0	61.1	32.0	8.3
stage2 or worse cancer	64.9	62.3	64.0	33.3	68.0	91.7

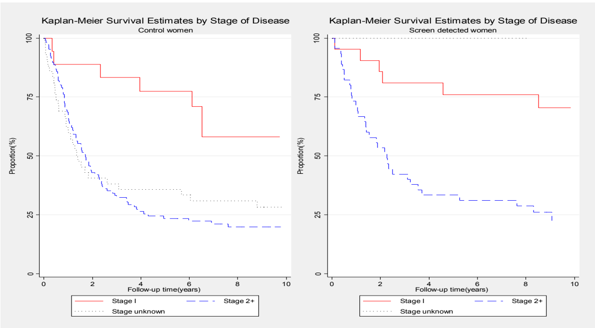

Figure 4. Screening Unaltered the Variation in Survival by Stage of Disease

(71.1% vs 18.8%). Within the screen-detected group, a higher survival estimate was observed among those with higher income than those with lower household income while the contrary was found for the cancer cases detected in the control group (Figure3). Figure4 shows the variation in survival by stage of disease. Table 2 describes the characteristics of women with respect to age at diagnosis.

Discussion

The comparison of survival estimates between screen-detected and control women showed that screening modified the survival of cervical cancer patients according to socio-economic factors. There was an increased variation in survival by different age groups and by type of houses if cancer was detected by screening. The variation in survival by education was reduced among screen-detected women while the survival pattern by occupation, marital status and household income were reversed if cancer was detected by screening. Variation in survival by stage of disease was more or less similar between screen-detected and control women.

The observed 5-year survival of women diagnosed with cervical cancer from the control arm was poor and the variation in survival according to socio-economic status was minimal, and was mainly due to the inadequate health care facilities in rural India and similar accessibility of health care facilities irrespective of socio-economic status. We were interested to see how survival was affected by the socio-economic factors if cancer was detected by screening and provided free treatment. We observed that the difference in survival between younger and older women increased substantially when cancer was detected by screening (20.8% *vs* 60% in screen-detected) while in control the survival difference was minimal (34% *vs* 29.1%). These findings also lead to an interesting question as of why survival was not improved in older women if cancer was detected by screening. In the same way the survival of women without education was found to be similar to that of survival of educated women if cancer was detected by screening whereas the survival of uneducated women was worse than educated women when cancer was diagnosed in the control arm. Women doing manual work, currently married, and with higher income had better survival than their counterparts if screen-detected, contrary to the observed survival pattern for women diagnosed with cancer from control arm.

Survival comparison between women diagnosed with cervical cancer from the control arm and the screen-detected women is not a good indicator to evaluate the screening effect because of over diagnosis, lead time and length bias (Sankila et al., 2000). The women with screen-detected cancers are bound to have good survival because the cancers are slow growing (length bias), and the time of diagnosis was advanced due to screening (lead time). Some screen-detected invasive cancers would not have been diagnosed during the women's lifetime without the screening activity. This over diagnosis is well known with screening e.g., for prostate and breast cancer (Gulati., 2014; Welch and Black, 2010). In the case of cervix cancer we do not have good evidence on over-diagnosis, but it would be unusual for cervix to be the only exception.

In fact we were not evaluating the screening effect by comparing the survival between screen-detected and women from control arm, but were trying to establish how screening was related to the variation in survival by background factors. Hence the good survival of women with screen-detected cancer is not an issue as such. Instead we were trying to illustrate who benefitted from screening in terms of improving the survival. The comparison of how the variation in survival by each of the background factors differs between cancer detected by screening and cancer diagnosed from control arm is credible because the biases probably affect all background factors of the screen-detected women in a similar way. Our study findings thus have an importance in describing the link between the selected socio-economic factors and cervical cancer survival with and without screening in this rural population.

A recent review on cervical cancer survival and older age suggests that the effect of age can be confounded by various patient, disease and treatment factors (Elit, 2014). In our study the proportion of women diagnosed with stage 1 cancers from the control arm did not vary much between women in different age groups but the younger and older women showed huge difference in the proportion of stage 1 cancers detected by screening (Table 2). That could be the major reason for such a big difference in the variation in survival by age at diagnosis between the two groups of women. Overall 19.4% of the screen-detected women (13/67) did not receive treatment. According to age at diagnosis, 19% from 30-39, 27% from 40-49 and 25% from 50+ year-old women did not receive treatment. But the treatment details were not available for the control women. Women diagnosed with cancer at an older age may be at a greater risk of death, which could also be due to other comorbidities. In our study the proportions of widowhood as well as no education were higher among older women (Table 2). Among screen-detected women, younger women had a better household income than the older while among women diagnosed with cancer from the control arm the older had a better household income. All these factors can influence women's decision making power, health seeking behaviors and attitude towards treatment. The older women need emotional and informational support from family members as well as the providers because information gaps and the stigma associated with diagnosis and treatment will affect the completion of their treatment and further follow-up (von Wagner et al., 2011).

In our previous study we found that women in all ages benefitted from screening in terms of reducing their risk for cervical cancer (Thulaseedharan et al., 2013). But in terms of survival women in all ages did not benefit from screening due to social and biological reasons. Manual workers and uneducated women benefitted most by utilizing free screening and treatment and reduced cervical cancer incidence among them (Thulaseedharan et al., 2013). In the case of survival also they benefitted because uneducated women attained the survival similar to that of educated women, and manual workers had a better survival than housewives. Widowed/separated women did not benefit from screening in terms of reducing the incidence of cervical cancer (Thulaseedharan et al., 2013). In the case of survival also they did not benefit because the widowed/separated women had significantly low survival compared to married women if cancer was detected by screening, and that could be again due to the effect of age and stage of disease.

Even if all screen-detected women were offered the same free treatment, there was a wide variation in survival by type of house in screen-detected compared to the control arm and this clearly indicates the role of socio-economic status in cervical cancer survival. We also found that women with lower household income had better survival rates than those with higher household income in the control arm, contrary to what was expected, while the reverse was observed if cancer was detected by screening. This contradictory finding in the control group might have been caused by misinformation from the self-reported participant income. Only 29% (48/165) of the women diagnosed with cervical cancer from control arm and 21% (14/67) of screen-detected women were reported to have a higher income and because of this small sample, chance observations (deaths) are also possible. However, such biases can happen in both groups of women in the same way and hence we cannot conclude that the contradiction is fully explained by misinformation or chance. One possible explanation is that married women reported the family income, which is higher than the income of single women. Among women from the control arm, survival of married women was worse than that for single women (31.3% *vs* 42.1). This supports the fact that the women with higher family income may not always have decision making power to seek health care. The better survival of married women among screen-detected could be due to the higher participation of married women in screening. They utilized the free screening and treatment and reduced the risk of developing cervical cancer (Thulaseedharan et al., 2013). We found that among the 67 screen-detected women about 34% of the married and 21% of widowed/separated women were diagnosed with stage 1 cancers. We also found that women from both income groups did not equally benefit from screening, with poor women having a poor survival compared to those with higher income.

In conclusion, In our previous study we found that background factors were associated with screening in terms of reducing the risk for cervical cancer (Thulaseedharan et al., 2013), and now we observe that background factors are also associated with screening in terms of variation in survival. Hence from our study we could strongly emphasize that cervical cancer survival is definitely connected with socio-economic factors. But the role of socio-economic factors in cervical cancer survival would differ according to the efficiency of health system. A hypothetical situation of good survival with no variation between background factors reflects the efficiency of health system, but poor survival with no variation between background factors reflects the inefficiency of health system. By analyzing the survival experience of women diagnosed with cancer from the routine care control arm and screen-detected women we could clearly illustrate the mechanism of the selected socio-economic factors in determining cervical cancer survival in this rural population. It is encouraging that screening improved the survival of uneducated and manual workers. Also the women diagnosed with stage 1 disease had a very good survival either detected by screening or diagnosed from control arm further stresses the importance of early detection of cervical cancer, and it is very encouraging in a public health point of view to implement cervical cancer control activities.

Acknowledgements

We acknowledge the Bill & Melinda Gates foundation for their financial support to our study through the Alliance for Cervical Cancer Prevention. Also we acknowledge Dr.Rama, Mr.Sampath and Mr.Selvakumar, Cancer Institute (WIA) Chennai for their help and support in data validation. The authors are grateful to Evelyn Bayle, Sandrine Montigny, and Krittika Guinot for their assistance in preparing this manuscript.

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