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Original Article

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Increased breast cancer incidence among nurses in a tertiary university hospital in South Korea

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ABSTRACT

Background: A series of breast cancer cases were recently reported in a tertiary university hospital in South Korea. Nurses are generally exposed to risk factors for breast cancer such as night shift work, antineoplastic agents, and job strain. However, the epidemiological evidence of excess incidence among nurses remains lacking. This study aims to investigate the excess incidence of breast cancer among nurses in a tertiary university hospital and provide epidemiological evidence of occupational risk factors.

Methods: A retrospective cohort was developed using personnel records of female workers in the nursing department who worked from January 2011 to June 2021 in a tertiary university hospital in South Korea. Sick leave records were used to identify cases of breast cancer. The standardized incidence ratio of breast cancer among nurses was compared to the general population.

Results: A total of 5,509 nurses were followed up for 30,404 person-years, and 26 breast cancer cases were identified. This study revealed a significantly increased breast cancer incidence among all included nurses, with a standardized incidence ratio of 1.65 (95% confidence interval [CI]: 1.08–2.41), compared to the general population. Workers, who handle antineoplastic agents in their representative department and current and/or former department, had significantly elevated breast cancer standardized incidence ratios of 2.73 (95% CI: 1.008–5.94) and 3.39 (95% CI: 1.46–6.68), respectively.

Conclusions: This study provides significant evidence of increased breast cancer risk among nursing staff in a hospital setting, particularly those who handle antineoplastic drugs. Measures that reduce exposure to risk factors should be implemented, especially anticancer drugs, to protect healthcare professionals. Further research at a national level that focuses on healthcare workers is necessary to validate breast cancer incidence and its contributing factors.

Keywords: Nursing staff; Health personnel; Breast neoplasms; Drug therapy; Antineoplastic agents

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Abbreviations

CI: confidence interval; IARC: International Agency for Research on Cancer; SIR: standardized incidence ratio.

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Competing interests

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Lee DW. Data curation: Lee DW. Formal analysis: Choi J. Funding acquisition: Lee DW, Hong YC. Investigation: Choi J. Methodology: Lee DW. Project administration: Lee DW, Hong YC. Supervision: Kim T. Validation: Lee DW. Writing - original draft: Choi J, Choi BY, Ryoo SW. Writing - review & editing: Lee DW, Hong YC.

BACKGROUND

Nurses could be exposed to various physical, chemical, and psychological hazards. Generally, occupational risk factors for breast cancer include ionizing radiation, electromagnetic fields, night shift work, ethylene oxide exposure, perfluorinated compounds, antineoplastic drugs, metals, and job strain.[1,2] Among these factors, night shift work, anticancer drug exposure, and job strain were identified as potential exposures through previously conducted in-depth interviews with the cases.

Recently, 4 workers in the department that handles antineoplastic agents in a tertiary university hospital were reported. The nursing department includes registered nurses and nurse assistants and represents the largest proportion of employees within the organization. The total workforce at the hospital accounted for 8,690 in 2020, including 2,922 (33.6%) working in the nursing department. Among them, the majority are females (n = 2,798), accounting for > 90%. Identifying harmful working conditions through these cases and accordingly establishing a safe working environment in the hospital is important because of the high proportion of the labor force.

An updated report by the International Agency for Research on Cancer (IARC) in 2019 on night shift work revealed an association with breast cancer, but epidemiological evidence in humans was lacking due to large heterogeneity among studies.[3,4] Meanwhile, a prospective cohort study that involves nurses revealed a significantly increased incidence of breast cancer among nurses who work night shifts for > 30 years.[5] Anticancer agents (e.g., busulfan, chlorambucil, cyclophosphamide, etoposide) demonstrated sufficient evidence to cause cancer in humans.[6] Epidemiological studies have revealed an excess incidence of cancer in nurses who handle antineoplastic drugs.[7,8] A Swedish study revealed an increased risk of breast cancer among women in full-time employment who experienced job strain,[9] but the association between breast cancer and job strain has been inconsistent among other studies.[10,11]

Some studies on the incidence or mortality of breast cancer among healthcare workers, including nurses, consistently revealed an increase in the risk of breast cancer.[12-14] In particular, a nationwide retrospective cohort study in Korea confirmed a significantly increased incidence of breast cancer among female healthcare workers in hospitals.[14] However, these studies evaluated nurses as a single group and did not differentiate or assess their risks separately.

Therefore, this study aimed to present epidemiological evidence of occupational risk factor exposure within a tertiary university hospital by investigating the excess incidence of breast cancer among employees in the nursing department and comparing them to the general population.

METHODS

Cohort definition

We used personnel records from the hospital to construct a retrospective cohort of nursing department workers in a tertiary university hospital in South Korea. . These records included demographic information (birth date and gender), work history (entry/exit dates and workplace), sick leave history (reason and start/end dates), and annual leave history (number of days and start/end dates). This study included female employees in the nursing department

who worked at the hospital from January 1, 2011, to June 30, 2021. This open cohort study enrolled newly hired employees during the cohort follow-up period as new study participants. This study excluded workers who were not affiliated with the Nursing Department or male workers. Finally, the cohort included a total of 5,509 qualified individuals.

The point of entry for those who joined the hospital before that date and the actual date of employment for those who joined afterward was January 1, 2011. The first sick leave due to breast cancer during the observation period was used as the cut-off point for follow-up observation, or the resignation date within the follow-up period for retired employees, or June 30, 2021, for the employees who remained even after that day.

Event definition

Sick leave records during the follow-up period defined breast cancer occurrence. The disease names in the records were inconsistently entered in both English and Korean, and a variety of terms for breast cancer were utilized. Therefore, cases were classified as breast cancer if they contained both words indicating a target organ (breast) and a target disease (cancer). The onset of breast cancer was the date of the first sick leave request due to breast cancer.

We applied no disease clearance period because we were unable to ascertain the occurrence of breast cancer before the cohort entry point. Further, we did not consider a latent period.

Workplace classification for exposure assessment

Of the occupational risk factors for breast cancer among nurses, night shift work, anticancer drug exposure, and job strain were identified as potential exposures through previously conducted in-depth interviews with the cases. This study used the workplace as a proxy for exposure to these risk factors because we could not directly evaluate the above-mentioned exposures.

Workers' representative workplace is where the worker served the longest during the follow-up period. The workplace was classified as "none" if the workplace was not listed in the personnel records during the follow-up period. The workplace could be tracked annually through personnel records, but mid-year changes could not be verified.

The representative workplaces were categorized based on four criteria: 1) workplaces that handle antineoplastic agents, including the hematology ward, and those related to anticancer treatment, versus other workplaces, 2) 4 classifications by main function: ward, outpatient/support, surgery/procedure/treatment, and emergency/intensive care, 3) annual leave usage by workplace: upper, middle, and lower thirds, and 4) average employee tenure by workplace: upper and lower 50%.

Workplaces that handle anticancer drugs were analyzed to understand the risk of work experience in these workplaces, associated with breast cancer incidence. The workplace used in personnel records may have been named for administrative convenience and may not accurately reflect the exact duties, thus the main tasks performed in each workplace were comprehensively considered, and the workplaces were categorized into four major functions. Furthermore, someone's absences were expected to minimally affect workplaces with high annual leave usage. Therefore, we used the annual leave usage of the workplace as an indirect workplace job demand indicator. Additionally, the average tenure of the workplace refers to the mixed effect of indirect risk factor exposure.

Furthermore, the use of their representative workplace as exposure could neglect their previous work experience, although that period would be relatively shorter. Therefore, the workers were classified based on their experience in a workplace that handles anticancer drugs after joining the hospital. This study defines a previous work experience as serving in a specific workplace in the personnel record, which was updated yearly. This, their record in the specific workplace in the specific year indicates that they worked in that workplace for at least ≥ 1 month in that year.

Statistical analysis

Indirect standardization methods were used to calculate age-standardized breast cancer incidence ratios because of the different age distributions among the groups.[15,16] Having prior knowledge of the incidence rates within the standard population is necessary. The expected number of cases within the study population can be calculated based on this information, and the ratio of observed cases to expected cases should be computed. We used the female population of the middle of 2015 from Statistics Korea as the standard population because the follow-up period was from January 1, 2011, to June 30, 2021. Age-specific breast cancer incidence in the general population was sourced from Cancer Statistics published by the Ministry of Health and Welfare in Korea. The standardized incidence ratio was calculated as the ratio of the observed number of cases in each representative workplace classification to the expected number of cases derived from each 5-year age group. A Poisson model was used to calculate the 95% confidence interval (CI) and significance level (*p*-value).[17] Further, the standardized incidence ratio (SIR) was calculated based on past work experience in specific workplaces to verify robustness. We provided the hospital with an Excel worksheet that would compute the age-SIR of breast cancer once the necessary data was inputted because raw data was inaccessible. We then received the summary statistics of the results. SAS STDRATE procedures (Version 9.3; SAS Institute INC., Cary, NC, USA) were used for statistical analysis.

Ethics statement

The Institutional Review Board (IRB) of Seoul National University Hospital waived the need for written informed consent to exempt the review of this study (IRB No. E-2109-032-1252).

RESULTS

The study cohort consisted of 5,509 workers, contributing to an overall observation time of 30,404 person-years, equating to an average observation period of 5.5 years per person. Their average age with standard deviation at entry to the hospital was 24.5 ±3.9 years and the average employment duration was 8.8 ± 8.8 years. We observed 26 cases of breast cancer during the follow-up period. The cohort primarily consisted of those born in the 1980s (44.4%) and 1990s (34.4%), followed by the 1970s (14.9%) and 1960s (4.4%). We classified the work assignments of 4,310 workers, thereby leaving 1,199 individuals unclassified due to missing workplace records.

Workers from workplaces that handle these agents accounted for 10.34% (n = 594) when representative workplaces were categorized into those handling antineoplastic agents and those who are not. Functional workplace categorization revealed that the largest group consisted of those working in the ward (39.0%, n = 2,151 of the total workforce), followed by those serving in emergency or intensive care units (17.5%, n = 964). Workers from outpatient/

Table 1. Descriptive statistics of the study participants

Characteristics	Values
Total	5,509 (100)
Birth year	
1950–1959	42 (0.8)
1960–1969	243 (4.4)
1970–1979	819 (14.9)
1980–1989	2,446 (44.4)
1990–1999	1,951 (35.4)
2000–2010	8 (0.2)
Department classification	
Ward	2,151 (39.0)
Outpatient/support	584 (10.6)
Surgery/procedure	611 (11.1)
Emergency/intensive care	964 (17.5)
Not classifiable	1,199 (21.8)
Handling antineoplastic drugs (representative department)	
Yes	594 (10.3)
No	3,716 (67.5)
Not classifiable	1,199 (21.8)
Handling antineoplastic drugs (cumulative experience)	
Yes	589 (10.7)
No	3,721 (67.5)
Not classifiable	1,199 (21.8)
Average days of annual leave used in the department	
Highest tertile	1,419 (25.8)
Middle tertile	1,862 (33.8)
Lowest tertile	1,029 (18.7)
Not classifiable	1,199 (21.8)
Average years of service of nurses in the department	
Upper 50 percentile (low turnover department)	916 (16.6)
Lower 50 percentile (high turnover department)	3,394 (61.6)
Not classifiable	1,199 (21.8)

Values are presented as number (%).

support and surgery/procedure/treatment workplaces have similar distributions of 584 (10.6%) and 611 (11.1%) individuals, respectively (**Table 1**).

Fig. 1 shows the characteristics of the 26 participants who were diagnosed with breast cancer. Of the 26 total cases, 9 (32.1%) were observed in outpatient workplaces. Both ward workers and surgery/procedure/treatment workers accounted for 21.8% each, consisting of 7 cases each. Additionally, we confirmed 2 cases in the emergency/intensive care workplace and 1 case among the unclassified worker group. Workers in the representative workplace that frequently handles anti-neoplastic agents accounted for 23.1% (6 cases) and the other workers were 76.9% (20 cases). The date of entry to the hospital was between July 1978 and November 2016, while the average working duration was 19.5 ± 7.3 years. The mean age at diagnosis was 42.5 ± 6.5 years.

The indirect standardization method was used to calculate SIRs, with the general population as a comparison group. The SIR of the total workers in the Nursing Department in the hospital was significantly elevated at 1.65 (95% CI: 1.08–2.41). The SIR was statistically significantly high at 2.73 (95% CI: 1.00–5.94) when we identified the representative workplace as frequently handling antineoplastic agents, and 3.39 (95% CI: 1.46–6.68) when we identified the cumulative experience on that workplace. However, workplaces that do not engage with antineoplastic agents reported SIRs of 1.45 (95% CI: 0.87–2.27) based on the representative workplace and 0.47 (95% CI: 0.77–2.11) based on the cumulative experience

No.	Classification	Handling antineoplastic drugs (representative workplace)	Year of entry	Working duration											Date of diagnosis	Age at diagnosis
				Total years	'11	'12	'13	'14	'15	'16	'17	'18	'19	'20	'21	
1	Ward	No	Jul-78	32.5												Jan-11	56.2
2	Outpatient/support	No	Sep-87	29.1												Nov-16	48.7
3	Outpatient/support	No	Sep-87	27.0												Oct-14	45.5
4	Ward	No	May-90	28.7												Jan-19	49.3
5	Surgery/procedure	Yes	Feb-94	27.3												May-21	52.0
6	Surgery/procedure	Yes	Mar-94	27.0												Mar-21	49.3
7	Emergency/intensive care	No	Apr-94	22.5												Sep-16	43.3
8	Surgery/procedure	No	Aug-94	24.0												Aug-18	46.9
9	Outpatient/support	No	Nov-94	26.7												Jul-21	48.9
10	Ward	Yes	Jul-96	16.7												Mar-13	42.0
11	Surgery/procedure	Yes	Aug-96	24.4												Jan-21	46.3
12	Outpatient/support	No	Nov-96	22.0												Oct-18	44.1
13	Emergency/intensive care	No	Mar-97	24.4												Jul-21	46.9
14	Ward	No	Nov-97	21.8												Sep-19	44.0
15	Outpatient/support	No	Jan-98	16.6												Aug-14	39.2
16	Outpatient/support	No	Aug-01	13.5												Feb-15	39.9
17	Outpatient/support	No	Sep-02	10.6												Apr-13	33.9
18	Ward	Yes	Dec-03	12.2												Feb-16	36.9
19	Outpatient/support	No	May-04	16.4												Oct-20	40.2
20	Outpatient/support	No	Mar-04	16.6												Feb-21	38.9
21	Surgery/procedure	Yes	Dec-04	16.0												Dec-20	41.4
22	Surgery/procedure	No	Dec-04	13.7												Aug-18	39.1
23	Ward	No	Apr-06	15.5												Jun-21	39.3
24	Not classifiable	No	May-06	10.0												May-16	33.2
25	Surgery/procedure	No	Feb-200	8.5												Aug-16	31.8
	Ward	No	Nov-16	3.4												Mar-20	28.2

Fig. 1. Characteristics of the observed breast cases.

(**Table 2**). Only the outpatient/support workplaces exhibited a significantly higher SIR at 2.41 (95% CI: 1.10–4.57) when we categorized the representative workplace into four major functions. Other functional categories were not significant. SIRs did not demonstrate significant differences among upper, middle, and lower groups when we categorized workers based on tertiles of annual leave usage by the workplace. The SIR was significantly higher for workers in workplaces in the upper 50% of average tenure at 2.46 (95% CI: 1.38–4.06) when we categorized the workers into the upper and lower 50% groups based on average tenure by workplace (**Table 2**).

DISCUSSION

We developed a retrospective cohort of 5,509 female nurses using personnel records from a tertiary university hospital. The comparison of breast cancer incidence in our study population to that of the general population revealed a higher incidence in the total study population (SIR: 1.65; 95% CI: 1.08–2.41) and among workers who handle antineoplastic agents (SIR: 2.73; 95% CI: 1.00–5.94).

Studies consistently revealed higher rates of breast cancer incidence among healthcare workers, including nurses. Rix and Lynge[12] investigated cancer incidence in Danish healthcare workers using census and cancer register records and revealed a high incidence of breast cancer among female registered nurses (SIR: 1.19; 95% CI: 1.08–1.30). A cohort study in Taiwan included physicians and revealed an increased breast cancer risk among females

Table 2. SIRs of nurses in a general tertiary hospital

Characteristics	Person-year	Observed cases	Expected cases	SIR (95% CI)	*p*
Total	30,404	26	15.78	1.65 (1.08–2.41)	0.0224
Classification of workplace					
Ward	14,019	7	6.88	1.02 (0.41–2.10)	0.9999
Outpatient/support	4,430	9	3.74	2.41 (1.10–4.57)	0.0290
Surgery/procedure	4,515	7	3.17	2.21 (0.89–4.55)	0.0856
Emergency/intensive care	5,680	2	1.5	1.33 (0.16–4.82)	0.8843
Not classifiable	1,760	1	0.49	2.02 (0.05–11.28)	0.7798
Handling antineoplastic drugs (representative Workplace)					
Yes	3,110	6	2.2	2.73 (1.008–5.94)	0.0498
No	25,534	19	13.09	1.45 (0.87–2.27)	0.1467
Not classifiable	1,760	1	0.49	2.02 (0.05–11.28)	0.7798
Handling antineoplastic drugs (cumulative experience)					
Yes	4,232	8	2.36	3.39 (1.46–6.68)	0.0060
No	508	17	0.47	1.32 (0.77–2.11)	0.3183
Not classifiable	1,760	1	0.49	2.02 (0.05–11.28)	0.7798
Average days of annual leave used in the workplace					
Highest tertile	6,782	7	5.31	1.32 (0.53–2.72)	0.5683
Middle tertile	12,024	11	5.79	1.90 (0.95–3.40)	0.0691
Lowest tertile	9,838	7	4.18	1.67 (0.67–3.45)	0.2615
Not classifiable	1,760	1	0.49	2.02 (0.05–11.28)	0.7798
Average years of service of nurses in the workplace					
Upper 50 percentile (low turnover)	7,008	15	6.1	2.46 (1.38–4.06)	0.0033
Lower 50 percentile (high turnover)	21,636	10	9.19	1.09 (0.52–2.00)	0.8740
Not classifiable	1,760	1	0.49	2.02 (0.05–11.28)	0.7798

SIR: standardized incidence ratio; CI: confidence interval.

(hazard ratio: 2.00; 95% CI: 1.11–3.62).[13] A study in Korea that used a nationwide health insurance database to construct a retrospective cohort of 107,646 female healthcare workers in hospitals revealed a significantly increased SIR for breast cancer compared to the entire worker population (SIR: 1.21, 95% CI: 1.09–1.36).[14] These results are congruent with our study findings, where the SIR for breast cancer in female workers in the nursing department as a whole was significantly higher at 1.65 (95% CI: 1.08–2.41).

Night shift work should be considered an occupational risk factor for breast cancer in nursing positions.[1] A meta-analysis study in Denmark revealed that the risk ratio between night shift workers for a relatively short period of < 8 years and general workers was 1.21, but with no statistical significance (95% CI: 0.97–1.32).[18] Other systematic reviews and meta-analysis studies revealed a relatively increased risk of breast cancer by 1.21–1.91 times with experience of night shift work, and the risk of breast cancer increases by approximately 3% for every additional 5 years of night shift work.[19] A prospective cohort study with 114,559 nurses in the United States revealed no significance in the breast cancer risk ratio of 0.94 for night shift nurses for 15–29 years (95% CI: 0.81–1.10), but the ratio was significantly higher at 1.40 (95% CI: 1.00–1.10) for those with > 30 years of night shift work.[5]

This study revealed that workers in the workplace with higher employment tenure have a higher risk of breast cancer incidence. The mixed effect of many potential risk factors for breast cancer among nurses explains this finding. The night work shift is one of the important factors in breast cancer occurrence. A high proportion of the subjects may have been exposed to night shift work, considering that 69.7% of nurses working in tertiary hospitals in Korea are known to work on a 3-shift basis according to nationwide survey results.[20] Therefore, as the average years of service of workers in the workplace increased,

their exposure to night shift work for a longer period is estimated to increase, which could affect breast cancer development.

Moreover, antineoplastic agents should be considered as occupational risk factors for breast cancer, to which the nurses in this study could have potentially been exposed. In 1979, Falck et al. in Finland reported significantly higher levels of mutagenic substances in the urine of nurses working with antineoplastic drugs compared to psychologists and office clerks.[7] A meta-analysis revealed cyclophosphamide detection in 11 out of 12 studies that analyzed the urine of nurses and other workers who handle antineoplastic drugs.[21] Additionally, a cohort study of 56,213 Canadian female nurses from 1974 to 2000 demonstrated epidemiological evidence of an increased risk of breast cancer among nurses who work in cancer centers or oncology nursing units.[7]

Our study did not measure biological antineoplastic drug exposure, but we confirmed that nurses, who predominantly handle these drugs, had a 2.73 times higher risk (95% CI: 1.00–5.94) of developing breast cancer compared to the general population. This trend was even more pronounced for nurses at the Oncology Daycare Center and Injections and Treatment Unit of the Cancer Hospital, where the risk surged as high as 12.90 times. A sensitivity analysis of workers who were previously employed in antineoplastic drug-handling workplaces revealed the robustly maintained risk of breast cancer at 8.54 times. These results indirectly indicate that antineoplastic drug exposure at worksites may contribute to breast cancer incidence. However, these results should be cautiously interpreted because of the shorter observation years of the study workplaces (342 person-years) compared to the total observation years (30,404 person-years), which might cause unstable ratio measurements.

The association between job strain and breast cancer has been inconsistent, but it is considered plausible. Some studies revealed no significant association between breast cancer and job strain.[10,11] However, a cohort study with 36,332 Swedish females defined a group with high job demand and low job autonomy as a group with high job strain. The group with high job strain had a significantly higher risk of breast cancer at 1.2 times.[9] Our study conducted a subgroup analysis based on the workplace's annual leave usage but revealed no significant association with breast cancer risk. This analysis hypothesized that annual leave usage indirectly shows the job demand in the workplace. However, qualitative research seems necessary to gain a more accurate understanding of the job demands of each workplace.

Breast cancer is more likely to be detected earlier with increased screening frequencies. This potentially introduces a detection bias that tends to increase the disease prevalence among nurses. Previous studies in Korea reported a breast imaging examination rate of 15.7% among nurses at 5 hospitals in 2002 and a 15.3% periodic breast mammography rate at another two hospitals in 2008,[22,23] which was notably lower compared to the national cancer screening rate of 33.2% and 49.3% in 2004 and 2008, respectively, among females aged > 40 years. A study in Taiwan revealed that < 10% of nurses reported being screened for breast cancer within the past 2 years in 2017, which is lower than the screening rate of 38.0% among general females aged 45–69 in 2015–2016.[24] Thus, these results confirmed that the screening rate of the breast cancer among our subjects was not significantly higher than the general population. Additionally, this study revealed that 53.8% of breast cancer was diagnosed in the 40s, which does not significantly differ from the epidemiologically confirmed prevalent age group in South Korea.[25] Considering these factors, we conclude a low likelihood of early detection bias due to frequent screening in the study population.

This study confirmed the excess risk of breast cancer by tracking and observing a considerable number of hospital staff in South Korea. The result, in comparison to the general population, is also meaningful despite the presence of the healthy worker effect, which can potentially bias results toward null. Previous studies have revealed higher breast cancer incidence and mortality rates among nurses in South Korea as a whole.[14,26] However, this study indirectly confirmed the risk of some occupational hazards (antineoplastic drugs, job strain, and night shift work) for breast cancer by understanding the characteristics of the affiliated workplaces and tasks within a single large tertiary hospital based on internal personnel data.

However, this study has several limitations. This study is based on the personnel records of a specific institution. A personnel record-based cohort cannot confirm the exposure to risk factors and medical history before the worker's admission, and tracking individuals after resignation is also impossible. Therefore, this study may be biased in both directions. Further, we were unable to adjust for individual factors, including reproductive history, familial history, hormone intake, smoking status, alcohol drinking,[27] and obesity, because information on such risk factors was unavailable. Additionally, we considered no disease clearance period due to a lack of data before cohort entry. Access to data with longer periods could generate more robust and comprehensive results in the future.

Our study applied no latent period because each occupational risk factor may have distinct latent periods. In particular, night shift work among nurses for > 30 years significantly increases the risk of breast cancer.[5] However, other risk factors included in our study contained no well-established information regarding their specific latent periods.

The anticancer drugs are known to be associated with the development of various cancer types, including acute myeloid lymphoma. However, this study did not comprehensively evaluate these potential associations.[28]

Confirming the exposure to risk factors requires additional methods, such as working environment measurement or biological monitoring, because the exposure to risk factors was not qualitatively evaluated, but categorized based on the workplace characteristics. The event definition might have a bias that converges toward null, as detection is only possible when the ill worker applies for sick leave. This causes missed cases or reports to be filed later than the actual diagnosis, thereby extending the follow-up time. However, this study revealed the very high incidence of breast cancer in workers from the workplace that handles antineoplastic drugs, which tends to have little effect on the study results.

We compared the risk of breast cancer incidence only to the general population. This result would become robust if we compared the subjects to another group, such as all female workers or female office workers in the same hospital. Alternatively, comparing the nursing staff with all employees within the hospital could have minimized the bias due to the healthy worker effect and enhanced comparability.

Finally, regional or institution-specific factors could influence our results that were drawn from a single university hospital, thus our results may not represent all healthcare institutions in the country. Future longitudinal studies that analyze the risk of cancer occurrence according to occupation and tasks among the Korean medical workforce are required through nationwide multi-institutional research.

CONCLUSIONS

This study significantly revealed that hospital employees in South Korea face an increased risk of developing breast cancer, particularly among nursing staff who handle antineoplastic drugs. Our results provide an essential step toward better understanding and managing the occupational risks of healthcare professionals. We recommend the implementation of comprehensive protective measures, such as rigorous procedures when handling antineoplastic drugs, reduced night shift schedules, and extensive job strain management programs, which may reduce the risk of breast cancer in hospital staff. Additionally, more regular and focused cancer screening programs should be implemented for staff who are exposed to higher occupational hazards. Further validation through nationwide studies is warranted to fully understand the depth of occupational hazards in the medical field and develop appropriate preventive strategies.

REFERENCES

1. Fenga C. Occupational exposure and risk of breast cancer. Biomed Rep 2016;4(3):282-92.
PUBMED | CROSSREF
2. Vainio H, Bianchini F. *Weight Control and Physical Activity*. Lyon, France: IARC Press; 2002.
3. Erren TC, Morfeld P, Groß JV, Wild U, Lewis P. IARC 2019: "Night shift work" is probably carcinogenic: what about disturbed chronobiology in all walks of life? J Occup Med Toxicol 2019;14(1):29.
PUBMED | CROSSREF
4. IARC Monographs Vol 124 group. Carcinogenicity of night shift work. Lancet Oncol 2019;20(8):1058-9.
PUBMED | CROSSREF
5. Wegrzyn LR, Tamimi RM, Rosner BA, Brown SB, Stevens RG, Eliassen AH, et al. Rotating night-shift work and the risk of breast cancer in the nurses' health studies. Am J Epidemiol 2017;186(5):532-40.
PUBMED | CROSSREF
6. Cogliano VJ, Baan R, Straif K, Grosse Y, Lauby-Secretan B, El Ghissassi F, et al. Preventable exposures associated with human cancers. J Natl Cancer Inst 2011;103(24):1827-39.
PUBMED | CROSSREF
7. Ratner PA, Spinelli JJ, Beking K, Lorenzi M, Chow Y, Teschke K, et al. Cancer incidence and adverse pregnancy outcome in registered nurses potentially exposed to antineoplastic drugs. BMC Nurs 2010;9(1):15.
PUBMED | CROSSREF
8. Falck K, Gröhn P, Sorsa M, Vainio H, Heinonen E, Holsti LR. Mutagenicity in urine of nurses handling cytostatic drugs. Lancet 1979;1(8128):1250-1.
PUBMED | CROSSREF
9. Kuper H, Yang L, Theorell T, Weiderpass E. Job strain and risk of breast cancer. Epidemiology 2007;18(6):764-8.
PUBMED | CROSSREF
10. Schernhammer ES, Hankinson SE, Rosner B, Kroenke CH, Willett WC, Colditz GA, et al. Job stress and breast cancer risk: the nurses' health study. Am J Epidemiol 2004;160(11):1079-86.
PUBMED | CROSSREF
11. Kruk J, Aboul-Enein HY. Psychological stress and the risk of breast cancer: a case-control study. Cancer Detect Prev 2004;28(6):399-408.
PUBMED | CROSSREF
12. Rix BA, Lynge E. Cancer incidence in Danish health care workers. Scand J Soc Med 1996;24(2):114-20.
PUBMED | CROSSREF
13. Lee YS, Hsu CC, Weng SF, Lin HJ, Wang JJ, Su SB, et al. Cancer incidence in physicians: a Taiwan National population-based cohort study. Medicine (Baltimore) 2015;94(47):e2079.
PUBMED | CROSSREF
14. Lee DW, Kim H, Lee W, Lee WR, Yoo KB, Choi JH, et al. Cancer incidence in Korean healthcare workers in hospitals. Cancers (Basel) 2023;15(7):2045.
PUBMED | CROSSREF

15. Breslow NE, Day NE. Statistical methods in cancer research. Volume II--The design and analysis of cohort studies. IARC Sci Publ 1987;82(82):1-406.
PUBMED

16. Sahai H, Khurshid A. *Statistics in Epidemiology: Methods, Techniques, and Applications*. Boca Raton, FL. USA: CRC Press; 1996.

17. Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology*. Philadelphia, PA, USA: Lippincott Williams & Wilkins; 2008, 776.

18. Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat 2013;138(1):291-301.
PUBMED | CROSSREF

19. Wang F, Yeung KL, Chan WC, Kwok CC, Leung SL, Wu C, et al. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. Ann Oncol 2013;24(11):2724-32.
PUBMED | CROSSREF

20. Korea Institute for Health and Social Affairs. *Healthcare Workforce Survey*. Sejong, Korea: Korea Institute for Health and Social Affairs; 2022.

21. Sessink PJ, Bos RP. Drugs hazardous to healthcare workers. Evaluation of methods for monitoring occupational exposure to cytostatic drugs. Drug Saf 1999;20(4):347-59.
PUBMED | CROSSREF

22. Lee SO, Sim ES, Ahn S. Factors affecting periodic screening behaviors for breast cancer among hospital nurses. Korean J Women Health Nurs 2010;16(4):390-8.
PUBMED | CROSSREF

23. Ju HO, Kim JS, Cho YS, Park NH, Eo YS, Cho YR, et al. A survey on cancer screening among nurses at General Hospital in Busan. Korean J Women Health Nurs 2003;9(1):18.
CROSSREF

24. Health Promotion Administration, Ministry of Health and Welfare. *2018 Annual Report of Health Promotion Administration*. Taipei City, Taiwan; 2018.

25. Kang SY, Lee SB, Kim YS, Kim Z, Kim HY, Kim HJ, et al. Breast cancer statistics in Korea, 2018. J Breast Cancer 2021;24(2):123-37.
PUBMED | CROSSREF

26. Shin Y, Kim UJ, Lee HA, Choi EJ, Park HJ, Ahn HS, et al. Health and mortality in Korean healthcare workers. J Korean Med Sci 2022;37(3):e22.
PUBMED | CROSSREF

27. International Agency for Research on Cancer (IARC). *IARC Handbooks of Cancer Prevention, Volume 15: Breast Cancer Screening*. Lyon, France: IARC; 2016.

28. International Agency for Research on Cancer (IARC). *Some Antiviral and Antineoplastic Drugs, and Other Pharmaceutical Agents*. Lyon, France: IARC; 2000.