International Journal of Biomedical Research
ISSN: 0976-9633 (Online); 2455-0566 (Print)
Journal DOI: 10.7439/ijbr
CODEN: IJBRFA

Original Research Article

Geographical Variation and Risk of Breast Cancer in Relation to ABO Blood Group System

Satyam Prakash[*1], Nand Kishore Sah[2], Khushbu Yadav[3] and Jitendra Kumar Singh[2]

[1]*Department of Biochemistry, Janaki Medical College Teaching Hospital, Tribhuvan University, Janakpurdham, Nepal*
[2]*Department of Community Medicine, Janaki Medical College Teaching Hospital, Tribhuvan University, Janakpurdham, Nepal*
[3]*Department of Microbiology, Krishna Medical Technical Research Center, Purwanchal University, Janakpurdham, Nepal*

*Correspondence Info:
Satyam Prakash
Assistant Professor,
Department of Biochemistry,
Janaki Medical College Teaching Hospital,
Tribhuvan University, Janakpur- 45600 Dhanusha, Nepal.
E-mail: sprakashy2424@gmail.com

Abstract

Background and Objectives: Breast cancer is the second most common malignancy which is a life threatening disease among young premenopausal women affecting their sexuality, femininity, body image, and maternal issues following mastectomy may lead the women to face psychiatric co-morbidity. Despite advancement and multifold improvement in scientific knowledge, at present there is no recognized method for primary prevention of breast carcinoma. Regional disparities in breast cancer outcomes have been reported in geographical variation and ABO blood group system which has also been associated with risk and survival for several malignancies. However, data for an association with breast cancer are inconsistent and contradictory too. Thus, the objective of this study was aimed towards geographical distribution and risk factors association of ABO blood antigen in breast cancer.

Methods: The data was collected from hospital records, patient's documents and annual reports which were verified with respective authorities. Collected data was analyzed by using SPSS 17.0 and was considered statistically significant at p-value ≤ 0.05. The adjusted Odds Ratios (OR) and 95% confidence Interval (CI) was also estimated.

Results: The risk of developing breast cancer differed significantly by ABO blood type in each of the two cohorts (p = 0.97) and this association between blood group and breast cancer risk was highly similar between the two independent populations. The adjusted risks of breast cancer associated with blood groups A, B, and AB were insignificant with risk factors for the disease. The association between ABO blood group and the subsequent risk of breast cancer was not modified to a statistically significant extent by age, BMI, age at menarche, menopausal status, marital status and smoking status.

Conclusion: The association between blood group and breast cancer risk was insignificant and is still controversial. Further studies are necessary to identify the mechanisms by which ABO blood type may influence the risk of breast cancer.

Keywords: Breast Cancer, ABO Blood Group, Menopause, Risk Factor, Insignificant,

1. Introduction

There is a marked geographical variation in the incidence of breast carcinoma worldwide in the developed and developing countries [1]. Breast Carcinoma is the most common cancer considered as a major public health problem leading to cause of death in women [2]. The incidence of breast cancer is 1 per 7 women and the probability of involvement is 12/5% during the lifetime. Globally, it is the most frequent malignant tumor, accounting 30 % of all malignancies and the second cause of mortality among females which occurs mainly in the peak of familial, social and economic activities in the age of 35–45 years [3].

Many factors have important role in the incidence of breast cancer such as genetic and non- genetic factors, endogenous hormones, lactation, reproductive history with nulliparity, late menopause, early at menarche and late age at first full time pregnancy is associated with increased risk [4-7]. The heritability of breast cancer is estimated about 30 % but known genetic risk variants such as BRCA1, BRCA2, TP53 and PTEN accounts 5–10 % of all cases [8, 9]. Non-genetic factors such as obesity, alcohol consumption, diet, radiation, birth weight and exposure to oestrogen have all been allied to breast cancer risk, but the mechanisms following these associations are yet to be identified [9]. Females commonly present with a lump in breast to a physician caused by different benign and malignant lesions [10, 11].

Since 19th Century, wide range of attempts has been made to determine a potential relationship between ABO and Rh blood groups and various metabolic and malignant diseases. The extensive findings acquired from studies on

patients with gastric cancer [12], salivary gland tumors [13], duodenal ulcer [14], colorectal cancer [15], thyroid disorders [16], ovarian tumors [17], Upper Urinary Tract tumors [18], small cell carcinoma of lung [19], breast cancer [20], pancreatic cancer [21], coronary heart disease [22, 23] and hypercholesterolemia [24] has shown association with ABO blood groups.

ABO blood group genes have a differential distribution in the population which is known as risk factor for development of diseases. It has been reported that several types of cancer are most evidently realistic in ABO and Rh blood group systems which are frequently used method nowadays [25]. Literature demonstrates several studies on blood groups classifying it into two groups: studies directly addressing blood groups and its genetics, and those addressing relationship between genetics of blood group and benign or malignant diseases [26].

Blood group antigens being the major antigen in humans are present on the surface of red blood cells and various epithelial cells. As the majority of human cancers are derived from epithelial cells, changes in blood group antigens are an important aspect of human tumor [27, 28]. In some tumors, alteration of ABO antigens is associated with malignant transformation [29]. ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. Thus, blood group antigen expression may be affected by genetic change of tumor [30].

Breast cancer mortality is higher in developing countries than in the developed countries [31]. Worldwide more than 20 million people are living with cancer and its number is expected to be more than 30 million by 2020 AD [32, 33]. According to the National Cancer Institute every two minutes one women is diagnosed with breast cancer and every 13 minutes a women dies of breast cancer in US [34]. According to World Health Organization (2011), breast cancer death in Nepal has reached 1,248 or 0.84% of total deaths [35]. Nepal ranks number 142 in the world and the age adjusted death rate is 12.92 per 100,000 of population. [36].

In Nepalese population, breast cancer is frequently seen in young age with late menarche, early first full-term pregnancy, a long duration of lactation and genetically inherited [37, 32]. There has been rapid increase in influx of people into municipal areas due to modernization and advancement in urban areas of Nepal. Life style changes like dietary habits, lack of physical exercise, less breast feeding by mothers are seen more frequently in urban women. These factors might contribute to an increased risk of breast cancer. Improvements in detection and treatment have increased survival rates and currently 85 % of women survive more than 5 years after diagnosis [32, 34]. However, breast cancer is still the most common cause of cancer death in the world with markedly increasing incidence [38].

Numerous reports have documented a relation between blood types and breast cancer incidence and prognosis [39]. Also, the tumor size, estrogen and progesterone receptor status and levels, tumor histology and the speed of cellular proliferation are some factors which affect the prognosis [40]. However, other studies have not found any relation between blood types and breast cancer [41-43]. In recent years, although there are published studies suggesting that blood groups are important in treatment response and prognosis in breast cancer. Also, regional disparities in breast cancer outcomes have been reported world widely. There is scarcity of data in this field [27, 44, 45]. Therefore, this study was focused to determine the geographical variation of breast cancer and to investigate the relationship between ABO blood groups with the risk of breast cancer.

2. Materials and Methods

2.1 Study Design and Area

This retrospective hospital based study was carried out at National Cancer Center, BP Koirala Memorial Cancer Hospital (BPKMCH), Bharatpur, Chitwan, Nepal in 2011 AD.

2.2 Study Population

A total of 283 confirmed diagnosed breast cancer patients were enrolled in this study.

2.3 Data Collection and Processing

A detailed demographic profile of the women like age, ABO blood group, Body Mass Index (BMI), marital status, age at menarche, menopausal status etc. was collected. A structured questionnaire and observational checklist was conducted to check for clarity prior to the main data collection period. Quantitative and qualitative data of histo-pathologically confirmed cases of breast cancer, laboratory data available for ABO blood type, detailed record of disease, course and history, patient's documents and annual reports were collected from medical record unit of BPKMCH hospital. The data collection was performed by the members of this research group and was cross checked by one another for any missed information.

2.4 Inclusion Criteria

Pathologically confirmed diagnosis of breast cancer, laboratory data available for ABO blood type and detailed record of disease, course and familial cancer history, oral contraceptive pills used and menopausal status were included.

2.5 Exclusion Criteria

The medical cancer outpatients and the ones receiving medical attention other than chemotherapy and patients whose blood groups were not registered in the record were excluded.

2.6 Statistical Analysis

The data obtained from secondary sources were edited reviewing the completeness, consistency and accuracy of the data; it was coded and entered into computer using SPSS 17.0 version. Percentage was used to see the relationship of distribution of the disease with regard to age, BMI, age at menarche, menopausal status, marital status and smoking status. The Chi-square test was used to test for the association of the various factors. The p-value ≤ 0.05 was considered statistically significant. Collected data was analyzed by using descriptive and inferential statistics. For each factor, the adjusted Odds Ratios (OR) and 95% confidence Interval (CI) was estimated.

2.7 Reliability and Validity

Consultation with DPHO/ DHO/ medical superintendent/ top authorities, literature review, participation in the meeting of DPHO and hospitals, seminar, frequent

supervision and cross checklist of the filled form were performed to maximize the reliability and validity of the study.

2.8 Ethical Consideration

The study was approved by ethical committee and Institutional Review board and Hospital committee of BPKMCH, Bharatpur, Chitwan prior to the study. Informed consent before interview from health professional and patients was taken by explaining the objective of the study. Strict confidentiality was also maintained for the information and documents collected through coding of questionnaire anonymously.

3. Results

3.1 Distribution of Subjects by Ecological and Developmental region

A total of 283 subjects had breast cancer, among them 190 were from Terai, 88 from Hills and 5 from Mountain region. Most of the subjects were found in Terai followed by hilly region. The highest number of respondents was found in both eastern and central development region of Terai with 34.73 % whereas in hilly region the highest number was found to be in western region with 38.63 %. The results are shown in table 1.

Table 1: Pattern of all study population

Developmental region	Ecological region			Total
	Terai (%)	Hill (%)	Mountain (%)	
Eastern	66 (34.73)	16 (18.18)	0 (0)	82
Central	66 (34.73)	24 (27.27)	0 (0)	90
Western	34 (17.89)	34 (38.63)	0 (0)	68
Mid- west	20 (10.52)	14 (15.90)	3 (60)	37
Far-west	4 (2.10)	0	2 (40)	6
Total	190	88	5	283

3.2 Baseline Characteristics of Study Subjects according to ABO Blood Type

Baseline characteristics of subjects in this study were highly similar across the four ABO blood groups. Most of the respondents had O blood group of median age, less than 25 kg/m^2 BMI, married and never smoke. The results are shown in table 2.

3.3 Distribution of ABO Blood Group and Rh Type among Subjects from Terai and Hill

The frequency distributions of ABO blood groups were nearly identical among subjects in the Terai and Hill. The risk of developing breast cancer differed significantly by ABO blood type in each of the two cohorts (p = 0.97) and this association between blood type and breast cancer risk was highly similar between the two independent populations. The results are shown in table 3.

Table 2: Baseline characteristics

Characteristics	Blood Group			
Subjects	**O**	**A**	**AB**	**B**
Terai	67	55	31	37
Hill	31	22	24	11
Total	98	77	55	48
Age				
Median (Years)	56.4	54.7	54.7	55.6
< 52 years (%)	20.0	26.6	25.6	22.4
52-70 years (%)	38.2	35.7	35.5	36.2
>70 years (%)	42.8	37.7	38.9	41.4
BMI				
Median (kg/m^2)	25.6	25.2	25.7	25.1
<25 kg/m^2 (%)	42.6	43.4	38.2	37.5
25-30kg/m^2 (%)	37.2	34.2	35.3	35.7
>30 kg/m^2 (%)	21.2	22.4	26.5	26.8
Age at Menarche				
Median (years)	13.8	14.3	14.1	14.3
<15 years (%)	52.5	47.8	48.9	41.4
15-17 years (%)	27.2	25.6	29.5	39.2
>17 years (%)	20.3	26.6	21.6	19.4
Menopausal Status				
Pre-menopausal (%)	32.6	33.3	35.2	38.9
Pos t-menopausal (%)	67.4	66.7	64.8	61.1
Marital Status				
Unmarried (%)	31.6	23.4	22.7	38.6
Married (%)	68.4	76.6	77.3	71.4
Smoking Status				
Never (%)	55.2	45.4	54.2	57.1
Past (%)	26.3	25.1	28.5	26.4
Current (%)	28.5	29.5	17.3	16.5

Table 3: Distribution of ABO blood group and Rh type

Blood Group	Terai	Hill	Total Study population
O	67	31	98
A	55	22	77
AB	31	24	55
B	37	11	48
Rh negative	42	19	61
Rh positive	148	69	217

3.4 Age Adjusted Multivariable–Adjusted Odds Ratios and 95 % Confidence Intervals for Breast Cancer by ABO Blood Type

The age-adjusted risks of breast cancer associated with blood groups A, B, and AB were not substantially altered by multivariable adjustment for other known or suspected risk factors for the disease. For the combined study population, compared with subjects with blood group O, those with blood groups A, AB or B were more likely to develop breast cancer (Age adjusted Odds ratios for breast cancer , 1.46 (95 % CI = 0.69 to 0.73), 1.54 (95 % CI = 0.79 to 0.89) and 1.73 (95 % CI = 0.78 to 0.99) respectively. The results are shown in table 4.

Table 4: Age adjusted multivariable –adjusted odds ratios and 95 % confidence intervals for breast cancer by ABO Blood type

Cohort	Blood Group			
Terai	**O**	**A**	**AB**	**B**
No of cases	67	55	31	37
Age Adjusted OR (95%CI)	1.00 (Referent)	1.54 (0.79 to 0.89)	1.56 (0.80 to 0.88)	1.68 (0.79 to 0.89)
Multivariable-Adjusted OR (95%CI)	1.00 (Referent)	1.57 (0.81 to 0.88)	1.58 (0.87 to 0.98)	1.68 (0.79 to 0.88)
Hill				
No of cases	31	22	24	11
Age adjusted OR (95%CI)	1.00 (Referent)	1.34 (0.78 to 0.89)	1.44 (0.79 to 0.89)	1.85 (0.79 to 0.89)
Muiltivariable Adjusted OR ((95%)	1.00 (Referent)	1.37 (0.65 to 0.69)	1.45 (0.82 to 0.84)	1.87 (0.81 to 0.88)
Total				
No of cases	98	77	55	48
Age adjusted OR (95% CI)	1.00 (Referent)	1.46 (0.69 to 0.73)	1.54 (0.79 to 0.89)	1.73 (0.78 to 0.99)
Multivariable –adjusted OR (95% CI)	1.00 (Referent)	1.46 (0.69 to 0.73)	1.57 (0.82 to 0.98)	1.74 (0.84 to 0.98)

3.5 Stratified Analysis of Breast Cancer by ABO Blood type

The association between ABO blood group and breast cancer risk differed according to Strata of other known or suspected risk factors. The association between ABO blood Group and the subsequent risk of breast cancer was not modified to a statistically significant extent by age, BMI, age at menarche, menopausal status, marital status and smoking status. The results are shown in table 5.

Table 5: Stratified Analysis of breast cancer

Characteristic	Blood Type HR (95% confidence interval)				
	O	**A**	**AB**	**B**	**P**
Age (years)					**0.34**
< 56 years	1.00 (Referent)	1.44 (0.34 to 0.89)	1.54 (0.77 to 0.89)	1.36(0.87 to 0.89)	
>56 years	1.00 (Referent)	1.14(0.87 to 0.78)	1.65 (0.67 to 0.79)	1.39 (0.87 to 0.89)	
BMI (Kg/m^2)					**0.74**
< 25	1.00 (Referent)	1.24 (0.67 to 0.89)	1.35 (0.67 to 0.89)	1.44 (0.87 to 0.89)	
>25	1.00 (Referent)	1.11 (0.87 to 0.81)	1.38 (0.57 to 0.89)	1.42 (0.87 to 0.89)	
Age at Menarche					**0.33**
<15 years	1.00 (Referent)	1.21 (0.77 to 0.89)	1.33 (0.77 to 0.89)	1.34 (0.87-0.89)	
>15 years	1.00 (Referent)	1.23(0.67 to 0.89)	1.44 (0.77 to 0.89)	1.23 (0.87 to 0.89)	
Menopausal Status					**0.23**
Pre-menopausal	1.00 (Referent)	1.35 (0.77 to 0.99)	1.51 (0.67 to 0.89)	1.54 (0.87 to 0.89)	
Post-menopausal	1.00 (Referent)	1.54 (0.77 to 0.89)	1.28 (0.87 to 0.89)	1.37 (0.87 to 0.89)	
Marital Status					**0.62**
Unmarried	1.00 (Referent)	1.34 (0.87 to 0.99)	1.76 (0.87 to 0.89)	1.37 (0.87 to 0.89)	
Married	1.00 (Referent)	1.64 (0.88 to 0.99)	1.11 (0.88 to 0.89)	1.32 (0.87 to 0.89)	
Smoking Status					**0.28**
Never	1.00 (Referent)	1.35 (0.84 to 0.89)	1.54 (0.79 to 0.89)	1.34 (0.87 to 0.89)	
Past or current	1.00 (Referent)	1.12 (0.83 to 0.99)	1.14 (0.87 to 0.89)	1.39 (0.87 to 0.89)	

P=Interaction

4. Discussion

Breast cancer in women is the main reason of too early cancer related mortality in Nepal. Despite the fact that the evaluation and treatment of patients is done as per western guidelines, there are substantial variations in risk factors, presenting stage and prognostic factors. Most Nepalese women are not aware of the risk factors associated with breast cancer [32]. The extensive studies have tried to investigate a possible relationship between ABO & Rh blood groups and breast cancer, yet the role of the ABO blood group in cancer remains controversial. The results have been proved as inconsistent and varied from one county to other. Many researchers have recognized the relationship between blood groups and breast cancer even though some studies shows no relationship [46,47].

The present study reveals the highest incidence of breast cancer was observed in Eastern and Central Development region of Terai than other regions of Nepal. The frequency distributions of ABO blood groups were nearly same among subjects in the Terai and Hill. Most of the respondents had O blood group followed by AB and others. Respondents who had leading breast cancer were found in median age group. This study also obtained most of the respondents had less BMI, age at menarche less than 15 years, married and never smoked. Similar findings were also obtained in the study conducted by Singh *et al* [32]. The increasing age is the most consistent and significant risk factor for breast cancer in female. Personal history and family history of breast cancer, nulliparity or late age at first childbirth, early menarche and late menopause, prior breast biopsy with hyperplasia or atypical hyperplasia, high breast tissue density, radiation exposure at a young age, alcohol consumption, and use of postmenopausal hormone therapy are other risk factors [48]. The risk of breast cancer increases exponentially up to the age of menopause, and the rate of increase in the risk slows significantly [49].

The present study highlights the association between blood type and breast cancer risk was highly similar between Terai and Hilly region respondents but the risk of developing breast cancer was found to be insignificant with ABO blood type ($p= 0.97$). Most of the respondents had Rh positive with breast cancer and was also found to be insignificant. Similar findings were also obtained from the study conducted by Akammu *et al* [47].

But, the association of breast cancer and the blood type had different degrees in various studies. The studies reported by Barbalic M *et al* and Paterson AD *et al* that blood group A may influence the systemic inflammatory response as they found associations between the genotype of the A blood group antigen and circulating levels of soluble intercellular adhesion molecule 1, E-selection and P Selection suggesting that increased incidence of breast cancer in blood group A cases [50,51]. On the other hand, blood group A individuals have a very low immunologic response to T and Tn antigens because they share the same sugar (N-acetylgalactosamine). This allows the cancer cells to bypass the immune system and replicate with little interference from the type A antibodies [52].

Saxena S *et al* reported the highest association of breast cancer in blood type A, least association with AB, B and slightly with O blood group in Jodhpur [53]. Luck G *et al* accounted in their study that A-blood group is more frequent in patients with breast cancer in comparison with O-blood group. They also highlights the risk of breast cancer in both familial and sporadic cases are related to the ABO blood group and the bilateral familial breast cancer has more prevalence in B-blood group than sporadic cases [54]. Iodice *et al* reported the incidence was higher among patients with O blood group and was statistically insignificant ($p=0.60$) [39]. A study performed by Holdsworth *et al* reported B or AB blood groups to be a prognostic factor for breast cancer [55]. Other studies observed positive associations with type A or B among women with a family history of breast cancer [21]. The significant associations between the blood type and risk of breast cancer were reported by Stamatakos M *et al* [56]. Yesmin *et al* noted the overall and disease-free survival was highest in O blood group followed by A blood group in breast cancer [57].

The risk of familial breast cancer was associated with the B blood group reported in the study conducted by Stamatakos *et al* [56]. Similarly, meta-analyses study was performed by Miao *et al* reported that the A blood group is associated with increased risk of breast cancer (OR: 1.12; 95% CI: 1.01–1.24) [27]. The high frequency of blood group A had been observed in breast cancer in the study conducted by Aly *et al* and Guleria *et al* [58, 59]. Blood group antigens are expressed on the surface of red blood cells and malignant breast ductal cells [60,61]. Alterations in ABO antigen expression on the surface of malignant cells have been observed for a variety of tumor types, including breast cancer [62]. The expression of blood group A has been reported to increase resistance to apoptosis and facilitate escape from immune control in rat colon carcinoma cells [63]. In addition, modified expression of blood group antigens on the surface of cancer cells may also alter cell motility with important implications for malignant progression [64]. This may be due to ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. As a consequence, blood group antigen expression may be affected by genetic change of tumor [59].

This study reports the combined study population of Terai and Hilly region, compared with subjects with blood group O, those with blood groups A, AB or B were more likely to develop breast cancer (Age adjusted Odds ratios for breast cancer, 1.46 (95 % CI = 0.69 to 0.73), 1.54 (95 % CI = 0.79 to 0.89) and 1.73 (95 % CI = 0.78 to 0.99) respectively. The adjusted risks of breast cancer associated with blood groups A, B, and AB were not substantially altered by

multivariable adjustment for suspected risk factors for the disease.

This study also observed the association between ABO blood group and the following risk of breast cancer was statistically insignificant by age, BMI, age at menarche, menopausal status, marital status and smoking status (p=0.34, 0.74, 0.33, 0.23, 0.62 and 0.28) respectively. While many studies have found an increased risk of breast cancer in postmenopausal women who are obese [65-67], others have found little or no association [46, 47]. Conversely, several case-control and cohort studies have linked obesity to a decreased risk of breast cancer in young women [68], which seems to have protective effect to reduce the risk of breast cancer by 34 to 60% and was found to be significant. [69,70]

Key and Pike suggested that the combination of estrogen plus progesterone induces mitosis of both normal and cancerous breast cells. Obesity in women who are in their reproductive age can create amenorrhea or inconsistent menstrual periods by shortening the luteal phase of the cycle, which occurs when progesterone is produced and mitosis occurs. This reduction in progesterone decreases the degree of breast cell mitosis, thereby producing a protective effect against breast cancer [71].

Similar type of study conducted by Stamatakos *et al* reported no positive correlation between age, family history, size of tumor, stage of malignancy, nodal metastasis or presence of progesterone/estrogen receptors and ABO blood groups system which is in accord with this study [56]. But the study conducted by Iodice *et al*, Klimant *et al*, Sozen and Benderli *et al*, Cihan *et al*, Miao *et al* in breast cancer, demographic characteristics such as age, menopausal status and ethnicity, tumor characteristics such as tumor size, axillary lymph node status, and histopathological subtype, and biomarkers such as oncogene, tumor suppressor genes, growth factors and proliferation measures are known to be potential prognostic factors [26,27,39,72,73].

5. Conclusion

The present study concluded that in two large independent cohorts, there was statistically significantly elevated risk for breast cancer among subjects with blood group antigens A or B compared with those with the blood group O. The highest risk was observed for participants with blood group B, the intermediate risks were observed for those with blood groups A and AB. The association between blood group and breast cancer risk was not statistically significantly modified by other known risk factors for the breast cancer. But, the evidence for association of blood groups with breast cancer is contentious, some study reported blood groups showed positive association [50,51] and others were negative [46,47]. The fact that there were discrepancies in the temporal data of blood group investigations regarding material, character, genetic and experimental applications indicates that blood groups remain to be mysterious related to breast cancer. However, further prospective studies are necessary to identify the mechanisms by which ABO blood type may influence the risk of breast cancer which will help to obtain consistent and concrete results.

Educational status and knowledge of the women in Nepal has a crucial value in the management of breast cancer. Screening and early detection programmes as Self Breast Examination (SBE) and clinical examination of the breast is recommended as complementary method of screening for women in the reproductive age group which should be extended throughout the country. A standard breast cancer treatment protocol should be followed by all the centers in country. Breast cancer awareness programs should be extended to the rural areas of Nepal where mass communication means are not adequate. Regular cancer education and appropriate trainings are important to physicians and nurses in order to improve the quality of cancer service to reduce the mortality rate and to enhance the health promotion.

Acknowledgement

Authors wish to acknowledge their cordial thanks to medical records units and concerned hospital authorities of BPKMCH, Bharatpur, Chitwan and Vth batch MBBS students of Janaki Medical College Teaching Hospital (JMCTH), Janakpur, Nepal for their charitable support, steady source of help and cooperation during this research.

References

[1] Ferlay J, Bray F, Pisani P, Parkin DM, GLOBANCAN 2002, Cancer incidence, mortality and prevalence worldwide. IARC Cancer base, Lyon: IARC Press; 2004. 5(2.0).

[2] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer.* 2010; 127: 2893–2917.

[3] Amini M, Fatah SH, Kalantari M. ABO blood groups and prognosis of breast cancer: a case-control study in Arak/Iran. *Iranian J of Blood and Cancer.* 2010; 1: 155-159.

[4] Lango D. Oncology and hematology. In: Harrison principles of internal medicine. 15th ed. Mc Graw- Hill, 2001 (1): 491-653.

[5] Colline CK. Pathologic basis of disease. 6th ed. Philadelphia: Saunders, 1999: 271-76, 1093-119.

[6] Rahimian M and Kheradmand AA. Principles of diagnosis and treatment of breast diseases. Tehran Iran: Partov: 2001.

[7] Griggs J, Desch CH. Solid Tumors. In: Cecil essentials of medicine.5th ed. Philadelphia: Saunders: 2004: 525-537.

[8] Claus EB, Schildkraut JM, Thompson WD, Risch NJ. The genetic attributable risk of breast and ovarian cancer. *Cancer.* 1996; 77(11): 2318–2324.

[9] Locatelli I, Lichtenstein P, Yashin AI. The heritability of breast cancer: a Bayesian correlated frailty model applied to Swedish twins data. *Twin Res*. 2004; 7(2): 182–191.

[10] Cottet V, Touvier M, Fournier A, Touillaud MS, Lafay L, Clavel-Chapelon F, *et al*. Postmenopausal breast

cancer risk and dietary patterns in the E3N-EPIC prospective cohort study. *Am J Epidemiol*. 2009; 170(10): 1257–1267.
[11] Pradhan M, Adhikari RC, Joshi A, Sigdel B, Basnet RB, Amatya V, *et al*. Present Cancer Status in T. U. Teaching Hospital, Nepal. *JSSN*. 1999; 2:13-23.
[12] Annual Report 2004 of BP Koirala Memorial Cancer Hospital; 2004. p. 7.
[13] Coon JS & Weinstein RS. Blood group-related antigens as markers of malignant potential and heterogeneity in human carcinomas, *Hum Pathol.* 1986; 17:1089-1086.
[14] Pinkston JA & Cole P. ABO blood groups and salivary gland tumors, *Cancer Causes Control*. 1990; 7: 572-574
[15] Li B, Tan B, Chen C, Zhao L, Qin L. Association between the ABO blood group and risk of common cancers. *J Evid Based Med*. 2014; 7(2): 79-83.
[16] Cao, X, Wen Z-S, Sun Y-J, Li Y, Zhang L, Han YJ. Prognostic value of ABO blood group in patients with surgically resected colon cancer, *British J Cancer.* 2014; 111: 174-180.
[17] Klechova L, Gosheva-Antonova TS, ABO and Rh blood group factors in thyroid gland diseases, *Vutr Boles.* 1980; 19:75-93
[18] Bjorkholm E. Blood group distribution in women with ovarian cancer. *Int J Epidemiol.* 1984; 13: 15-17.
[19] Kvist E, Lauritzen AF, Bredesen J, Luke M. Relationship between blood groups and tumors of the upper urinary tract, *Scand J Urol Nephrol.* 1988; 22(4): 289-291.
[20] Cerny T, Fey MF, Oppliger R, Nachbur B, gertsh M. Prevalence of Rhesus negative phenotypes in Caucasian patients with small cell lung cancer, *Int J Cancer.* 1992; 52: 504-506.
[21] Anderson DE & Haas C. Blood Type A and Familial Breast Cancer, *Cancer.* 1984; 54: 1845- 1849.
[22] Vioque & Walker AM. Pancreatic cancer and ABO blood types: a study of cases and controls. *Med Clin.* 1991; 96(20): 761-764.
[23] Sharif S, Anwar N, Farasat T, Naz S. ABO blood group frequency in Ischemic heart disease patients in Pakistani population, *Pak J Med Sci.* 2014; 30(3): 593-595.
[24] Lee HF, Lin YC, Lin CP, Wang CL, Chang CJ, Hsu LA. Association of blood group A with coronary artery disease in young adults in Taiwan, *Intern Med.* 2012; 51(14): 1815-1820.
[25] Jassim WE. Association of ABO blood group in Iraqis with hypercholesterolaemia, hypertension and diabetes mellitus, East Mediterr. *Health J.* 2012; 18(8): 888-891.
[26] Klimant E, Glurich I, Mukesh B, Onitilo A. Blood type, hormone receptor status, HER2/neu status, and survival in breast cancer: a retrospective study exploring relationships in a phenotypically well-defined cohort. *Clin Med Res.* 2011; 9: 111-118.
[27] Miao Su-Yu, Zhou W, Chen L, *et al*. Influence of ABO blood group and Rhesus factor on breast cancer risk: a meta-analysis of 9,665 breast cancer patients and 244,768 controls. *Asia Pac J Clin Oncol*. 2013 [Epub ahead of print].
[28] Dabelsteen E, Gao S. ABO blood-group antigens in oral cancer. *J Dent Res*. 2005; 84(1): 21-8.
[29] Coon JS, Weinstein RS, Blood group-related antigens as markers of malignant potential and heterogeneity in human carcinomas, *Hum. Pathol*. 1986; 17: 1089-1086.
[30] Su M, Lu SM, Tian DP, Zhao H, Li XY, *et al*. Relationship between ABO blood groups and carcinoma of esophagus and cardia in Chaosan inhabitants of China. *World J Gastroenterol*. 2001; 7: 657–661.
[31] Nakagoe T, Nanashima A, Sawai T, Tuji T, Ohbatake M, Jibiki M, *et al*. Expression of blood group antigens A, B and H in carcinoma tissue correlates with a poor prognosis for colorectal cancer patients. *J Cancer Res Clin Oncol.* 2000; 126(7): 375–82.
[32] Singh Y, Sayami P, Sayami G, Nakagawa H, Kooreeda T. Nepalese Breast Cancer in Relation to Reproductive Factors: Comparision between Nepalese and Japanese cases. *Anticancer Research.* 2002; 22: 319- 324.
[33] Singh YP, Sayami P, Management of Breast Cancer in Nepal, IOM TUTH, Kathmandu, Nepal. *J Nepal Med Assoc*. 2009; 48: 252-7.
[34] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA: A Cancer Journal for Clinicians.* 2005; 55: 74-108.
[35] Cancer facts and figures, Atlanta; American Cancer Society. 2009.
[36] http://www.worldlifeexpectancy.com/nepal-breast-cancer
[37] Bhattacharya S and Adhikari S. Evaluation of risk factors, diagnosis and treatment in carcinoma breast-a retrospective study. *Kathmandu Univ Med J.* 2006; 4: 54-60.
[38] Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. International Agency for Research on Cancer; 2013. [http://globocan.iarc.fr]
[39] Iodice S, Maisonneuve P, Botteri E, Sandri MT, Lowenfels AB. ABO blood group and cancer. *Eur J Cancer*. 2010; 46: 3345-3350.
[40] Gates MA, Xu M, Chen WY *et al*. ABO blood group and breast cancer incidence and survival. *Int J Cancer*. 2012; 130: 2129-2137.
[41] Unal D, Eroglu C, Kurtul N *et al*. ABO blood groups are not associated with treatment response and prognosis in patients with local advanced non- small cell lung cancer. *Asian Pac J Cancer Prev.* 2013; 14: 3945-3948.
[42] Ürün Y, Utkan G, Yalcin S *et al*. Lack of any relationship between ABO and Rh blood groups and clinicopathological features in patients with gastrointestinal stromal tumors: Turkish Oncology Group. *Asian Pac J Cancer Prev*. 2013; 14: 4129-4131.
[43] Utkan G, Ürün Y, Cangir AK, *et al*. Clinicopathological features of patients with malignant mesothelioma in a multicenter, case-control study: no role for ABO-Rh blood groups. *Asian Pac J Cancer Prev*. 2013; 14: 249-253.
[44] Klimant E, Glurich I, Mukesh B, Onitilo A. Blood type, hormone receptor status, HER2/neu status, and survival in breast cancer: a retrospective study exploring relationships in a phenotypically well-defined cohort. *Clin Med Res*. 2011; 9: 111-118.
[45] Gates MA, Xu M, Chen WY, Kraft P, Hankinson SE, Wolpin BM. ABO blood group and breast cancer incidence and survival. *Int. J. Cancer*. 2012; 130(9): 2129–2137.
[46] Aird I, Bentall HH, Mehigan JA, Roberts JA. The blood groups in relation to peptic ulceration and carcinoma of colon, rectum, breast, and bronchus; an association between the ABO groups and peptic ulceration. *Br Med J.* 1954; 2: 315-321.

[47] Akammu AS, Durusinmi–E FAA, Emuveyan EE. Abdol-Kaareem FB, Vgwoude CS, Dawotola DA. The Association between cancer of the breast and ABO and Rhesus D antigen phenotypes in Lagos, Nigeria. Central study. *Nigerian J. of Clinical Practice*. 2002; 5(2): 81-86.

[48] Colditz GA. Epidemiology and prevention of breast cancer. *Cancer Epidemiol Biomarkers Prev*. 2005; 14: 768-772.

[49] Smigal C, Jemal A, Ward E, Cokkinides V, Smith R, Howe HL *et al*. Trends in breast cancer by race and ethnicity. *CA Cancer J Clin.* 2006; 56: 106-130.

[50] Barbalic M, Dupuis J, Dehghan A, Bis JC, Hoogeveen RC *et al*. Largescale genomic studies reveal central role of ABO in sP-selectin and sICAM-1 levels. *Hum Mol Genet.* 2010; 19: 1863-1872.

[51] Paterson AD, Lopes-Virella MF, Waggott D, Boright AP, Hosseini SM *et al*. Genome-wide association identifies the ABO blood group as a major locus associated with serum levels of soluble E-selectin. *Arterioscler Thromb Vasc Biol*. 2009; 29: 1958-1967.

[52] Dean L. Blood Groups and Red Cell Antigens [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2005. In: The ABO blood group. Available from: http://www.ncbi.nlm.nih.gov/books/NBK2267/

[53] Saxena S, Chawla KV, Gupta KK and Gaur LK. Association of ABO blood group and breast cancer in Jodhpur. *Indian J Physiol Pharmacol.* 2015; 59(1): 63–68.

[54] Luck G, Haber ND, Adams P. Blood type and cancer. 2005, 14 (4): 308 -312.

[55] Holdsworth WJ, Benson EA, Clayden AD. Blood group as prognostic indicator in breast cancer. *Br Med J*. 1995; 290 (6469): 671-673.

[56] Stamatakos M, Kontzoglou K, Safioleas P, Safioleas C, Manti C, Safioleas M. Breast cancer incidence in Greek women in relation to ABO blood groups and Rh factor. *Int. Semin. Surg. Oncol*. 2009; 6: 14.

[57] Yasemin Benderli Cihan, Significance of ABO-Rh Blood Groups in Response and Prognosis in Breast Cancer Patients Treated with Radiotherapy and Chemotherapy, *Asian Pacific Journal of Cancer Prevention.* 2014; 15, 2014: 4055-4060.

[58] Aly R, Yousef A, Elbably O. Association of ABO Blood Group and Risk of Breast Cancer. *J Blood Disorders Transf*. 2014; 5: 241.

[59] Guleria K, Singh H, Kuar, Sambyal V. ABO blood group in gastrointestinal tract (GIT) and Breast Carcinoma Patients. *Anthropologist.* 2005; 7: 189-192.

[60] Yazer MH. What difference 2 nucleotides make: a short review of ABO genetics. *Transfus Med Rev.* 2005; 19: 200-209.

[61] Strauchen JA, Bergman SM, Hanson TA. Expression of A and B tissue iso-antigens in benign and malignant lesions of the breast. *Cancer.* 1980; 45: 2149- 2155.

[62] Hakomori S. Antigen structure and genetic basis of histo-blood groups A, B and O: their changes associated with human cancer. *Biochim Biophys Acta*. 1999; 1473: 247-266. International Agency for Research on Cancer. http://globocan.iarc.fr

[63] Marionneau S, Le Moullac-Vaidye B, Le Pendu J. Expression of histoblood group A antigen increases resistance to apoptosis and facilitates escape from immune control of rat colon carcinoma cells. *Glycobiol.* 2002; 12: 851-856

[64] Le Pendu J, Marionneau S, Cailleau-Thomas A, Rocher J, Le Moullac-Vaidye B *et al*. ABH and Lewis histo-blood group antigens in cancer. *APMIS*. 2001; 109: 9-31.

[65] Helmrich SP, Shapiro S, Rosenberg L *et al*. Risk factors for breast cancer. *Am J Epidemiol* 1983; 117: 35-45.

[66] De Waard F, Baanders-Van Halewijn EA. A prospective study in general practice on breast-cancer risk in postmenopausal women. *Int J Cancer*. 1974; 14: 153-160.

[67] Barnes-Josiah D, Potter JD, Sellers TA *et al*. Early body size and subsequent weight gain as predictors of breast cancer incidence (Iowa, United States). *Cancer Causes Control*. 1995; 6:112-118.

[68] Hunter DJ, Willett WC. Diet, body size, and breast cancer. *Epidemiol Rev.* 1993; 15:110-132.

[69] Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev*. 1993; 15: 36-47.

[70] Willett WC, Browne ML, Bain C *et al*. Relative weight and risk of breast cancer among premenopausal women. *Am J Epidemiol* 1985; 122: 731-735.

[71] Key TJ, Pike MC. The role of oestrogens and progestagens in the epidemiology and prevention of breast cancer. *Eur J Cancer Clin Oncol.* 1988; 24: 29-13.

[72] Sozen S, Benderli Cihan Y. Tumor characteristics, treatment and survivial periods of elderly patients with breast cancer in elderly. *Turkish J Geriatrics.* 2012; 15: 164-70.

[73] Cihan YB, Baykan H, Kavuncuoglu E *et al*. Relationships between skin cancer and blood groups-link between non-melanomas and ABO/Rh factors. *Asian Pac J Cancer Prev*. 2013; 14: 4199-4203.