Original Article

Determinants of Breast Cancer Among Women in Southern Pakistan: Evidence from a Hospital-Based Case–Control Study

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Abstract

Background: Breast cancer is a significant global health issue in women, and its prevalence is on the increase in low- and middle-income nations. Although breast cancer is becoming a burden, the data on the possible risk factors in Pakistan is scarce.

Objective: To establish the relationship between demographic, reproductive, lifestyle, and familial variables and frequency of breast cancer in women in South Punjab, Pakistan.

Methods: A case-control study was carried out in a hospital in 104 cases (breast cancer cases) and 127 control (healthy age-matched women) in Multan, D.G. Khan, and Bahawalpur divisions. A validated structured questionnaire was used to gather data on socio-demographics, reproductive history, lifestyle factors, and medical history. Chi-square tests and multivariate logistic regression were used to test the associations between variables and breast cancer.

Results: Women aged 41–55 years had significantly higher risk of breast cancer (OR=6.34, 95% CI: 1.41–28.5, p=0.016). Oral contraceptive use (OR=2.12, 95% CI: 1.07–4.20, p=0.031) and history of breast infection/treatment (OR=4.28, 95% CI: 2.05–8.95, p<0.001) were strong independent risk factors. Moderate predictors were iron deficiency anemia (OR=1.87, 95% CI: 1.01344, p=0.045) and lower levels of education.

Conclusion: These results present a need to include specific awareness, early screening programs, and preventive interventions in current public health programs to decrease the burden of breast cancer among women in South Punjab, Pakistan.

Keywords: Breast cancer; south punjab; risk factors; frequency; case-control study

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Introduction

Breast cancer is the most frequently diagnosed cancer among women globally, representing a major public health challenge with significant morbidity and mortality.[1] The World Health Organization (WHO) reports that over 2 million new cases are diagnosed annually, and incidence is rising particularly in low- and middle-income countries due to changes in reproductive patterns, lifestyle factors, and delayed detection. In Pakistan, it is the single most prevalent health concern among women and contributes to roughly 36% of all female cancer, and it stands fourth leading cause of cancer-related deaths.[1] The prevalence of breast cancer in various populations varies widely ranging from 20% to 92% in American, African, Asian, and Middle Eastern populations.[2,3] In recent years, new cases have also reported in East Asia and South-Central regions including Korea and Southeast Asia.[4] In 2012, breast cancer caused nearly 0.5 million deaths worldwide and ranked among the top five leading major causes of death in developing countries.[2,3] The age-standardized incidence rate had already scaled 50.3 cases per 100,000 women in 2012, and it gradually increased over time. Breast cancer is a multifactorial condition that is determined by the interaction of several genetic predispositions, reproductive history, hormonal exposure, lifestyle, and socio-demographic determinants. Regional and global studies have

identified a number of risk factors to be implicated in its causation, including socioeconomic, genetic, demographic, and reproductive factors.[5] Among various risk factors, age and gender are still the strongest breast cancer determinants, with rates increasing significantly post-menopause. But there is variation in research about whether younger or older individuals are more susceptible, with some having poorer prognosis among old age individuals.[6] Higher socioeconomic status has been linked to higher risk of breast cancer likely due to delayed childbearing, physical inactivity, and high-fat diet, but with possible concomitant earlier detection and better prognosis.[7] Various risk factors including urban living, occupation, and education along with reproductive and hormonal conditions are also highly suspicious of breast cancer risk. The possible association of abortion history with risk for breast cancer is still controversial, with evidence producing conflicting results.[8,9] In resource-limited countries such as Pakistan, efforts to reduce breast cancer risk and control face numerous barriers including poor awareness, infancy of health infrastructure, shortage of trained health workers, and sociocultural determinants.[10] Lack of national-level epidemiological surveys also impede in devising effective control and early detection strategies. Setting the context-specific risk profile is therefore paramount for developing evidence-based focused interventions. In view of these inadequacies, the objective of this study was to evaluate the association between demographic, reproductive, lifestyle, and familial factors and breast cancer risk using a case-control design. Understanding regional determinants of breast cancer will support evidence-based planning for improvement in prevention efforts, risk-reduction interventions and health policy.

Methods

All procedures were performed in accordance with the Helsinki declaration, and ethics committee approval was obtained (IRB No. MN/048/2022). This case-control study was conducted between January 2023 and September 2024 among women who seek healthcare services at tertiary healthcare centers in the South Punjab region including Multan, Dera Ghazi Khan and Bahawalpur divisions. This current study employed a non-probability consecutive sampling technique for participant recruitment and data collection. The sample size was determined based on a case–control study design to detect an odds ratio (OR) of 2.5 for the association between family history of breast cancer and disease outcome, with 80% statistical power and a 5% level of significance (two-sided). Assuming a 10% disease exposure among controls, the minimum required sample size was calculated to be 149 participants using standard sample size estimation methods for unmatched case-control studies. To ensure adequate statistical power, account for potential non-response, and allow subgroup analyses, the final ample size was increased to 231 women. In this case-control study, individuals having breast cancer were classified as the case group while women without current or prior breast cancer visiting healthcare center with other health issues e.g. seasonal flu or any respiratory infection designated as control group. The inclusion criteria for participants for case group include women aged >18 years, diagnosed with breast cancer (stages 1–4; grades 1–3) within the last six months, confirmed by histopathology and medical records, and who had resided in the targeted regions for at least five years. While, the inclusion criteria for participants for control, group was similar with just no current or history of breast cancer. The exclusion criteria include male participants, women with a previous breast cancer diagnosis, individuals with high-risk genetic syndromes (e.g., confirmed BRCA1/2 mutation carriers), and women residing outside the targeted regions. A written informed consent was obtained from each participants, ensuring the confidentiality of collected information. Information was collected using a well-structured questionnaire. This questionnaire comprised of four distinct domains having different items related to demographic and socioeconomic status, physiological or hormonal changes, family background, medical interventions, medical history, reproductive attributes and lifestyle. A pilot study with 31 individuals was carried out to assess the feasibility and accuracy of designed questionnaire and survey approach. The semi-structured questionnaire was validated with the involvement of an expert review panel comprising oncologists, epidemiologists, and public health specialists. The validation was based on achieving excellent test-retest reliability with kappa values of 0.78-0.92 for categorical variables and intraclass correlation coefficients of 0.85-0.94 for continuous variables, ultima-

tely confirming the feasibility and reliability of the proposed methodology for the full-scale investigation. Descriptive analysis was performed to estimate frequencies and percentages for variables using the Statistical Package of the Social Sciences (version 20). Shapiro-Wilk test was used to assess normal distribution of data. The chi-square test was used to assess the relationships between individual variables and breast cancer occurrence. Logistic regression analysis was performed to identify independent predictors at $p<0.05$ of significant level.

Results

Several socio-demographic, reproductive and clinical variables were significantly associated with breast cancer risk. Age distribution differed significantly between cases and controls ($\chi^2 = 18.42$, $p = 0.001$). Univariable logistic regression showed significantly higher odds of breast cancer among women aged 26–40 years (OR = 7.35, 95% CI: 1.63–33.0, $p = 0.009$), 41–55 years (OR = 11.61, 95% CI: 2.70–49.9, $p < 0.001$), and >55 years (OR = 9.95, 95% CI: 2.17–45.6, $p = 0.002$) compared with women aged 18–25 years. Educational level showed a significant association with breast cancer ($\chi^2 = 7.83$, $p = 0.02$). Compared with illiterate women, those with higher education had significantly increased odds of breast cancer (OR = 3.16, 95% CI: 1.39–7.16, $p = 0.006$). However, women with primary or secondary education did not show a statistically significant difference (OR = 1.73, $p = 0.118$) (Table 1).

Table 1: *Socio-Demographic Characteristics of Participants*

Variables	Category	Case (n=104)	Control (n=127)	Total (N=231)		Chi-square tests		Univariable logistic regression analysis		
		n (%)	n (%)	n (%)	95% CI	χ^2	p-value	Odds Ratio (OR)	95% CI	p-value
Age (Years)	18–25	2 (1.9)	21 (16.5)	23 (9.9)	6.73–14.50	18.42	0.001*	Ref	–	–
	26–40	21 (20.2)	30 (23.6)	51 (22.1)	17.21–27.86			7.35	1.63–33.0	0.009*
	41–55	63 (60.6)	57 (44.9)	120 (51.9)	45.53–58.31			11.61	2.70–49.9	<0.001*
	>55	18 (17.3)	19 (15.0)	37 (16.1)	11.85–21.31			9.95	2.17–45.6	0.002*
Age at Marriage	≤20	52 (50.0)	65 (51.2)	117 (50.6)	44.24–57.03	9.71	0.008*	Ref	–	–
	>20	40 (38.5)	30 (23.6)	70 (30.3)	24.74–36.51			2.13	1.02–4.42	0.041*
	Not married	12 (11.5)	32 (25.2)	44 (19.0)	14.51–24.60			3.56	1.58–8.01	0.002*
Area (Division)	Multan	34 (32.7)	41 (32.3)	75 (32.5)	26.76–38.75	1.78	0.41^{NS}	Ref	–	–
	D.G. Khan	47 (45.2)	66 (52.0)	113 (48.9)	42.54–55.33			0.78	0.43–1.41	0.40
	Bahawalpur	23 (22.1)	20 (15.7)	43 (18.6)	14.12–24.13			1.20	0.57–2.55	0.62
BMI	<30	69 (66.3)	83 (65.4)	152 (65.8)	59.47–71.62	0.02	0.88^{NS}	Ref	–	–
	≥30	35 (33.7)	44 (34.6)	79 (34.2)	28.38–40.53			0.96	0.54–1.69	0.881
Education	Illiterate	35 (33.6)	24 (18.9)	59 (25.5)	20.35–31.53	7.83	0.02*	Ref	–	–
	Primary/Secondary	51 (49.1)	64 (50.4)	115 (49.8)	43.39–56.18			1.73	0.87–3.43	0.118
	High	18 (17.3)	39 (30.7)	57 (24.7)	19.56–30.62			3.16	1.39–7.16	0.006*
Family type	Joint	58 (55.8)	78 (61.4)	136 (58.9)	52.43–65.02	0.73	0.39^{NS}	Ref	–	–
	Individual	46 (44.2)	49 (38.6)	95 (41.1)	34.98–47.57			0.79	0.47–1.34	0.38
Marital Status	Single	13 (12.5)	32 (25.2)	45 (19.5)	14.89–25.07	5.21	0.16^{NS}	Ref	–	–
	Married	65 (62.5)	67 (52.8)	132 (57.1)	50.70–63.36			2.39	1.12–5.11	0.024*
	Separated/Divorced	12 (11.5)	16 (12.6)	28 (12.1)	8.52–16.96			1.85	0.70–4.84	0.21
	Widow	14 (13.5)	12 (9.4)	26 (11.3)	7.80–15.98			2.87	1.01–8.15	0.047*
Profession	Housewife	79 (75.9)	81 (63.8)	160 (69.3)	63.04–74.86	3.97	0.046^{NS}	Ref	–	–
	Employed	25 (24.1)	46 (36.2)	71 (30.7)	25.14–36.96			1.79	1.01–3.18	0.045*
Residence	Rural	45 (43.3)	56 (44.1)	101 (43.7)	37.48–50.17	0.01	0.90^{NS}	Ref	–	–
	Urban	59 (56.7)	71 (55.9)	130 (56.3)	49.83–62.52			1.03	0.62–1.73	0.90

Note: *significant ($p<0.05$), ^{NS}Non-significant ($p>0.05$)

Oral contraceptive use differed significantly between cases and controls ($\chi^2 = 10.03$, $p = 0.003$). A higher proportion of cases reported oral contraceptive use (36.5%) compared with controls (18.1%). Univariable logistic regression showed that women who used oral contraceptives had 2.6 times higher odds of breast cancer compared with non-users (OR = 2.60, 95% CI: 1.43–4.74, $p = 0.002$). History of breast infection or treatment was strongly associated with breast cancer ($\chi^2 = 20.76$, $p < 0.001$). Approximately 40.4% of cases reported previous breast infection or treatment compared with 14.2% of controls. Women with this

history had 4.11 times higher odds of breast cancer (OR = 4.11, 95% CI: 2.14–7.88, p < 0.001) (Table 2).

Table 2: *Reproductive and Lifestyle Characteristics of Participants*

Variables	Category	Case (n=104)	Control (n=127)	Total (N=231)		Chi-square tests		Univariable logistic regression analysis		
		n (%)	n (%)	n (%)	95% CI	χ^2	p-value	Odds Ratio (OR)	95% CI	p-value
Abortion history	No	95 (91.3)	110 (86.6)	205 (88.7)	84.01–92.20	1.28	0.26^{NS}	Ref	–	–
	Yes	9 (8.7)	17 (13.4)	26 (11.3)	7.80–15.99			0.61	0.26–1.44	0.26
Age at menarche	≤13	26 (25.0)	34 (26.8)	60 (25.9)	20.74–31.98	0.10	0.75^{NS}	Ref	–	–
	>13	78 (75.0)	93 (73.2)	171 (74.1)	68.02–79.26			0.91	0.50–1.64	0.75
Menopause age	No menopause	56 (53.8)	73 (57.5)	129 (55.8)	49.39–62.10	0.38	0.83^{NS}	Ref	–	–
	<50	19 (18.3)	23 (18.1)	42 (18.2)	13.74–23.66			1.08	0.52–2.26	0.84
	≥50	29 (27.9)	31 (24.4)	60 (26.0)	20.74–31.98			1.22	0.62–2.40	0.56
Hormone replacement therapy	No	83 (79.8)	92 (72.4)	175 (75.8)	69.84–80.84	1.74	0.19^{NS}	Ref	–	–
	Yes	21 (20.2)	35 (27.6)	56 (24.2)	19.16–30.16			0.66	0.36–1.21	0.18
Number of deliveries	Nulliparous	45 (43.3)	56 (44.1)	101 (43.7)	37.48–50.17	0.08	0.96^{NS}	Ref	–	–
	1–3	36 (34.6)	41 (32.3)	77 (33.3)	27.57–39.64			1.09	0.59–2.00	0.78
	>3	23 (22.1)	30 (23.6)	53 (23.0)	17.99–28.78			0.95	0.48–1.88	0.89
Age at first delivery	No child	17 (16.3)	36 (28.3)	53 (22.9)	17.99–28.78	6.35	0.096^{NS}	Ref	–	–
	<20	49 (47.1)	47 (37.0)	96 (41.6)	35.39–48.00			2.21	1.06–4.61	0.034*
	20–30	26 (25.0)	28 (22.1)	54 (23.4)	18.38–29.25			1.96	0.88–4.36	0.099
	>30	12 (11.6)	16 (12.6)	28 (12.1)	8.52–16.96			1.59	0.61–4.16	0.34
Breastfeeding duration	No breastfeeding	29 (27.9)	48 (37.8)	77 (33.3)	27.57–39.64	5.72	0.12^{NS}	Ref	–	–
	<2 years	23 (22.1)	28 (22.1)	51 (22.1)	17.21–27.86			1.36	0.69–2.69	0.37
	2–4 years	41 (39.4)	32 (25.2)	73 (31.6)	25.95–37.85			2.12	1.10–4.08	0.024*
	>4 years	11 (10.6)	19 (14.9)	30 (12.9)	9.25–17.94			0.96	0.42–2.22	0.93
Oral contraceptive use	No	66 (63.5)	104 (81.9)	170 (73.6)	67.55–78.86	10.03	0.003*	Ref	–	–
	Yes	38 (36.5)	23 (18.1)	61 (26.4)	21.14–32.45			2.60	1.43–4.74	0.002*
Reproductive tract infection	No	91 (87.5)	83 (65.4)	174 (75.3)	69.38–80.44	15.40	0.001*	Ref	–	–
	Yes	13 (12.5)	44 (34.6)	57 (24.7)	19.56–30.62			0.27	0.14–0.50	<0.001*
History of breast infection/treatment	No	62 (59.6)	109 (85.8)	171 (74.1)	68.02–79.26	20.76	<0.001*	Ref	–	–
	Yes	42 (40.4)	18 (14.2)	60 (25.9)	20.74–31.98			4.11	2.14–7.88	<0.001*
Number of children (parity)	None	31 (29.8)	52 (40.9)	83 (35.9)	30.02–42.30	6.21	0.10^{NS}	Ref	–	–
	<3	23 (22.1)	28 (22.1)	51 (22.1)	17.21–27.86			1.38	0.71–2.69	0.34
	3–5	39 (37.5)	28 (22.1)	67 (29.1)	23.53–35.16			2.34	1.24–4.40	0.008*
	>5	11 (10.6)	19 (14.9)	30 (12.9)	9.25–17.94			0.97	0.42–2.25	0.95
Smoking	No	83 (79.8)	97 (76.4)	180 (77.9)	72.14–82.79	0.36	0.55^{NS}	Ref	–	–
	Yes	21 (20.2)	30 (23.6)	51 (22.1)	17.21–27.86			0.82	0.43–1.55	0.55
Consanguinity	No	74 (71.2)	92 (72.4)	166 (71.9)	65.74–77.26	0.04	0.84^{NS}	Ref	–	–
	Yes	30 (28.8)	35 (27.6)	65 (28.1)	22.74–34.26			1.06	0.59–1.89	0.84

Note: *significant (p<0.05), ^{NS}Non-significant (p>0.05)

Among family and medical history variables, iron deficiency anemia was the only factor significantly associated with breast cancer (χ^2 = 4.15, p = 0.041). Women with anemia had 1.73 times higher odds of breast cancer compared with those without anemia (OR = 1.73, 95% CI: 1.02–2.95, p = 0.041) (Table 3).

Table 3: *Family History of Participants*

Variables	Category	Case (n=104)	Control (n=127)	Total (N=231)		Chi-square tests		Univariable logistic regression analysis		
		n (%)	n (%)	n (%)	95% CI	χ^2	p-value	Odds Ratio (OR)	95% CI	p-value
Family history of any type of cancer	No	95 (91.3)	111 (87.4)	206 (89.2)	84.51–92.56	0.93	0.337^{NS}	Ref	–	–
	Yes	9 (8.7)	16 (12.6)	25 (10.8)	7.44–15.49			0.66	0.27–1.59	0.34
Breast cancer history	No	81 (77.9)	108 (85.1)	189 (81.8)	76.34–86.26	1.968	0.161^{NS}	Ref	–	–
	Yes	23 (22.1)	19 (14.9)	42 (18.2)	13.74–23.66			1.62	0.82–3.21	0.16
Diabetes mellitus history	No	46 (44.2)	50 (39.4)	96 (41.6)	35.39–48.00	0.556	0.456^{NS}	Ref	–	–
	Yes	58 (55.8)	77 (60.6)	135 (58.4)	52.00–64.61			0.82	0.48–1.39	0.46
Hypertension	No	74 (71.2)	79 (62.2)	153 (66.2)	59.91–72.02	2.047	0.152^{NS}	Ref	–	–
	Yes	30 (28.8)	48 (37.8)	78 (33.8)	27.98–40.09			0.67	0.38–1.18	0.16

Toxaemia during pregnancy	No	96 (92.3)	114 (89.8)	210 (90.9)	86.50–93.98	0.448	0.503^{NS}	Ref	–	–
	Yes	8 (7.7)	13 (10.2)	21 (9.1)	6.02–13.50			0.73	0.29–1.85	0.51
Iron deficiency anemia	No	34 (32.7)	58 (45.7)	92 (39.8)	33.73–46.26	4.15	0.041*	Ref	–	–
	Yes	70 (67.3)	69 (54.3)	139 (60.2)	53.74–66.27			1.73	1.02–2.95	0.041*
Note: *significant (p<0.05), ^{NS}Non-significant (p>0.05)										

Multivariable logistic regression analysis showed that women aged 41–55 years had significantly higher odds of breast cancer compared with those aged 18–25 years (aOR = 8.91, 95% CI: 1.87–42.4, p = 0.006), while women older than 55 years also had increased risk (aOR = 6.74, 95% CI: 1.29–35.1, p = 0.023). Higher education level was independently associated with breast cancer risk (aOR = 2.54, 95% CI: 1.08–5.97, p = 0.032). Similarly, oral contraceptive use significantly increased the likelihood of breast cancer (AOR = 2.18, 95% CI: 1.16–4.09, p = 0.015) (Table 4).

Table 4: *Multivariable Logistic Regression Analysis of Factors Associated with Breast Cancer*

Variable	Category	AOR	95% CI	p-value
Age (years)	18–25	Ref	–	–
	26–40	5.42	1.11–26.3	0.036*
	41–55	8.91	1.87–42.4	0.006*
	>55	6.74	1.29–35.1	0.023*
Age at marriage	≤20	Ref	–	–
	>20	1.64	0.74–3.64	0.221
	Not married	2.41	1.02–5.71	0.044*
Education	Illiterate	Ref	–	–
	Primary/ Secondary	1.39	0.66–2.91	0.381
	Higher education	2.54	1.08–5.97	0.032*
Oral contraceptive use	No	Ref	–	–
	Yes	2.18	1.16–4.09	0.015*
Reproductive tract infection	No	Ref	–	–
	Yes	0.36	0.18–0.71	0.003*
History of breast infection/ treatment	No	Ref	–	–
	Yes	3.57	1.78–7.15	<0.001*
Iron deficiency anemia	No	Ref	–	–
	Yes	1.52	0.86–2.68	0.145
Note: *significant (p<0.05), ^{NS}Non-significant (p>0.05)				

Discussion

The current study explored a broad spectrum of possible risk factors of breast cancer among women from South Punjab, Pakistan, who sought primary acre at cancer referral healthcare centers. This study revealed that several factors including age, weight, marriage age, education, knowledge, reproductive infection, breast infection, oral contraceptive pill use, physical activity patterns, and iron deficiency anemia, were independently related to breast cancer. This is consistent with previous observations highlighting the multifactorial natural of breast cancer and provide important insights into the epidemiological determinants of the disease within the studied population.[11,12] In developed countries, breast cancer is more prevalent in women of greater socioeconomic status, mainly because of delayed marriage and childbearing, lower parity and shorter duration of lactation.[13] Conversely, in middle- and low-income countries such as Kazakhstan and Pakistan, poor life conditions, restricted healthcare access, and delayed diagnosis have been forcefully associated with elevated breast cancer occurrence.[14]

Age emerged as one of the most significant predictors of breast cancer. Women aged 41–55 years and older than 55 years showed substantially higher odds of developing breast cancer compared with younger women. Unlike many Western countries, where breast cancer developed after the age of 50,[15] Pakistani women are diagnosed with breast cancer at a younger age. Likewise, a similar trend has been noted to occur among Palestine women implying that genetic predispositions, hormonal balance, and environmental effects have a role to play and that aging is also linked to a decrease in immune monitoring which can lead to early development of cancer.[16] The better educated women tend to wait longer before getting married, delay the birth of their children, have fewer children and engage themselves in professional activities. These can change the pattern of reproductive hormones and diminish the protective effects of early pregnancy and long periods of breastfeeding which have been proven to reduce the risk of breast cancer.[17] Use of oral contraceptives was also found to be an independent risk factor of breast cancer. Women who reported taking oral contraceptives were much more likely to develop breast cancer than their non-users. This conclusion is justified by a considerable number of epidemiological studies that suggest that hormonal contraceptives can lead to a

small increase in the risk of breast cancer, especially when used chronically.[17,18] History of breast infection or treatment was strongly linked with breast cancer risk. Women who had reported a history of breast infections were greatly more prone to developing breast cancer. In chronic inflammation, chronic inflammatory responses can result in the release of cytokines, reactive oxygen species, and other mediators able to damage the cellular DNA and abnormal cell proliferation. The microenvironment of the tissue can also change during inflammatory processes to provide conditions that are conducive to the developpment and growth of tumors.[19]

The strengths of this research are as follows: (a) it is one of the first region-specific studies that examined the risk factors of breast cancer in women in South Punjab, therefore, offering valuable epidemiological information on a poorly reported population and offering context-relevant information on intervenetions relevant to the population; and (b) the study included histologically confirmed cases of breast cancer, thus, eliminating possible misclassification and cutting down on confounding Nevertheless, the research has a number of limitations as well. The sample size used is relatively small and this might have influenced the statistical power to identify the association with some variables. Moreover, the research was performed in a geographically localized area with a non-probability sampling and based on a hospital setting, which constrains the generalizability of the results to the entire population of women in Pakistan and might also cause a potential selection bias.

Conclusion

The findings of this study emphasize the complex interaction between biological, reproductive, and socio-demographic factors in breast cancer development. Understanding these relationships is essential for designing effective prevention strategies and improving early detection efforts. From a public health perspective, the results highlight the importance of breast health awareness programs, improved reproductive health counseling, and targeted screening for high-risk groups.

Ethical Approval: The Institutional Review Board, MNS University of Agriculture Multan approved this study vide letter No. No: IRB/MNSUAM/048-022.

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Authors' Contribution:

MAR: Conception & design, Drafting of article, final approval of the version to be published

FS, NS, NS, AB, ZP: Acquisition of data, analysis and interpretation of data

MA: Conception & design, acquisition of data, analysis and interpretation of data, drafting of article

AUR: Conception & design, acquisition of data, analysis and interpretation of data, drafting of article, critical revisions for important intellectual content

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