



Effect of XRCC1 Gene Polymorphism (rs1799782) on Response and Toxicities of Chemotherapy in Bangladeshi Breast Cancer Patients



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Background

- Breast cancer remains a major health concern in Bangladesh, with chemotherapy being a cornerstone of treatment.
- The XRCC1 gene plays a crucial role in DNA repair, and its polymorphism (rs1799782) may influence chemotherapy response and toxicities.
- Genetic variations in DNA repair genes have been linked to differential treatment outcomes, making pharmacogenomic studies essential for optimizing cancer therapy.

Objectives

- This study aims to evaluate the impact of XRCC1 (rs1799782) polymorphism on chemotherapy response and treatment-induced toxicities in Bangladeshi breast cancer patients, providing insights into personalized treatment strategies.

Breast Cancer



- Breast cancer is one of the most prevalent malignancies worldwide and a leading cause of cancer-related mortality among women.
- In Bangladesh, the burden of breast cancer is rapidly increasing, attributed to genetic, environmental, and lifestyle factors.
- Genetic mutations that compromise DNA repair pathways are critical contributors to breast carcinogenesis, as they lead to genomic instability and uncontrolled cell proliferation.
- Among the DNA repair genes, the X-ray repair cross-complementing group 1 (XRCC1) gene plays an indispensable role in the base excision repair (BER) pathway, which is responsible for correcting single-strand DNA breaks resulting from oxidative stress, alkylation, and other endogenous or exogenous DNA-damaging agents.

Epidemiology

- The 5 year survival rate for localized breast cancer has increased from 72% in the 1940's to 97 percent today.
- Regionally spread cancer drops the rate to 78%
- Distant metastases drops the survival rate even lower to 23%

Epidemiology

International Agency for Research on Cancer

World Health Organization

Male

Female

Western Europe

Northern America

Northern Europe

Australia/New Zealand

Southern Europe

More developed regions

Polynesia

South America

Micronesia

Central and Eastern Europe

Caribbean

World

Northern Africa

Western Asia

Melanesia

Southern Africa

Western Africa

South-Eastern Asia

Central America

Less developed regions

Eastern Africa

South-Central Asia

Eastern Asia

Middle Africa

100 80 60 40 20 0 20 40 60 80 100

Incidence
Mortality

GLOBOCAN 2012 (IARC)

International Agency for Research on

World Health Organization

Breast

Cervix uteri

Oesophagus

Gallbladder

Lip, oral cavity

Ovary

Stomach

Lung

Other pharynx

Colorectum

Liver

Corpus uteri

Non-Hodgkin lymphoma

Leukaemia

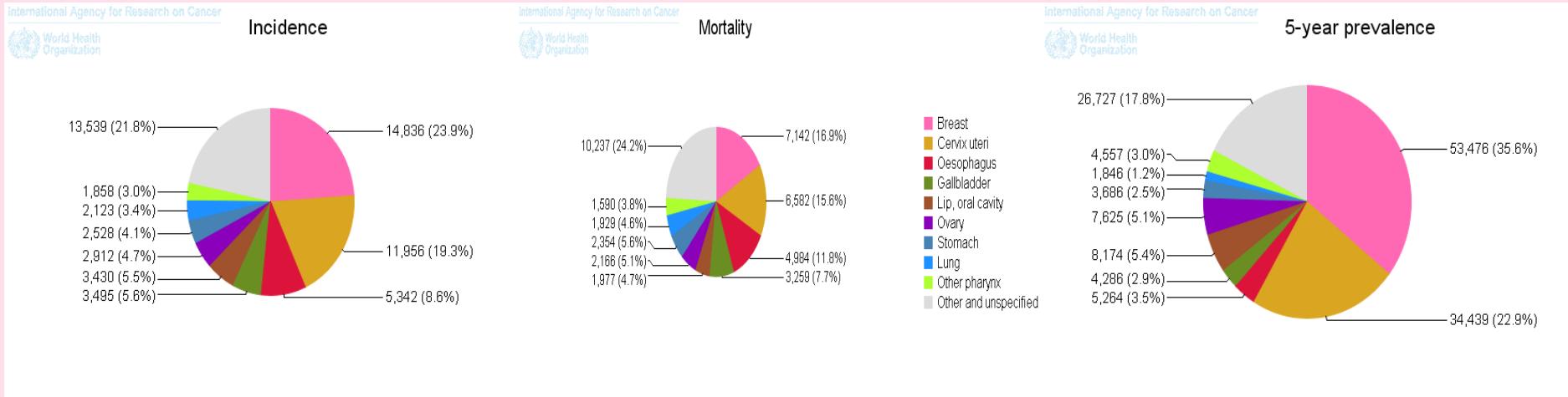
Thyroid

Incidence
Mortality

0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30

ASR (W) rate per 100,000

Epidemiology



Treatment Individualization

- Currently, several lines of evidence support the utility of pharmacogenomics that associate specific genetic polymorphisms in drug metabolizing enzymes (e.g., GSTPT1, PMT, UGT1A1, DPD), drug transporters (ABCB1, ABCC4, MRP1), and drug target enzymes (TS) with clinical outcomes in patients treated with commonly prescribed chemotherapy drugs, such as 5-FU and irinotecan (Lee et al., 2005).
- The ultimate goal of these genetic and pharmacogenetic studies is to enable the selection of the treatment that is most likely to provide benefit and minimal toxicity to patients

Treatment Specification

- Total number of patient: 400
- No. of patient receiving neoadjuvant chemotherapy: 182
- No. of patient receiving adjuvant chemotherapy: 218
- **Drugs used:** Cyclophosphamide-Epirubicin-5-Fluorouracil (CEF)/ Cyclophosphamide-Doxorubicin (Adriamycin)-5-Fluorouracil (CAF)
- **Dose:** Cyclophosphamide: 500mg/m²
Epirubicin / Doxorubicin: 80mg/m²
5-Fluorouracil: 500mg/m²

*Patients are assessed in every three weeks

Response Assessment

Response Evaluation Criteria in Solid Tumors (RECST) (Therasse et al.,2000)

Complete Response (CR): Disappearance of tumor for at least four weeks

Partial Response (PR): At least a 30% decrease of the longest diameter of tumor for more than 4 weeks

Progressive Disease (PD): At least a 20% increase of the longest diameter of tumor

Stable Disease: Neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease

Toxicity Evaluation

- The sixth edition of American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging System (Greene et al., 2002)
- Common Terminology Criteria for Adverse Events (CTCAE v3.0)(Cancer Therapy Evaluation Program, 2003).

General Toxicity: Patients with grade I, II

Severe Toxicity: Patients with grade III, IV

XRCC1

- X-ray repair cross-complementing protein 1 (XRCC1) is an essential DNA repair protein in humans, encoded by the XRCC1 gene. It plays a crucial role in the base excision repair (BER) pathway, facilitating the repair of single-strand breaks in DNA.
- XRCC1 functions as a scaffold protein, interacting with key DNA repair enzymes such as DNA ligase III, DNA polymerase β , and poly (ADP-ribose) polymerase 1 (PARP1) to coordinate efficient repair processes.
- XRCC1 plays a crucial role in the metabolism and DNA repair response to cyclophosphamide, an alkylating agent widely used in chemotherapy. Cyclophosphamide induces DNA cross-links and single-strand breaks, which require efficient repair mechanisms to maintain genomic integrity.

Pharmacogenetics

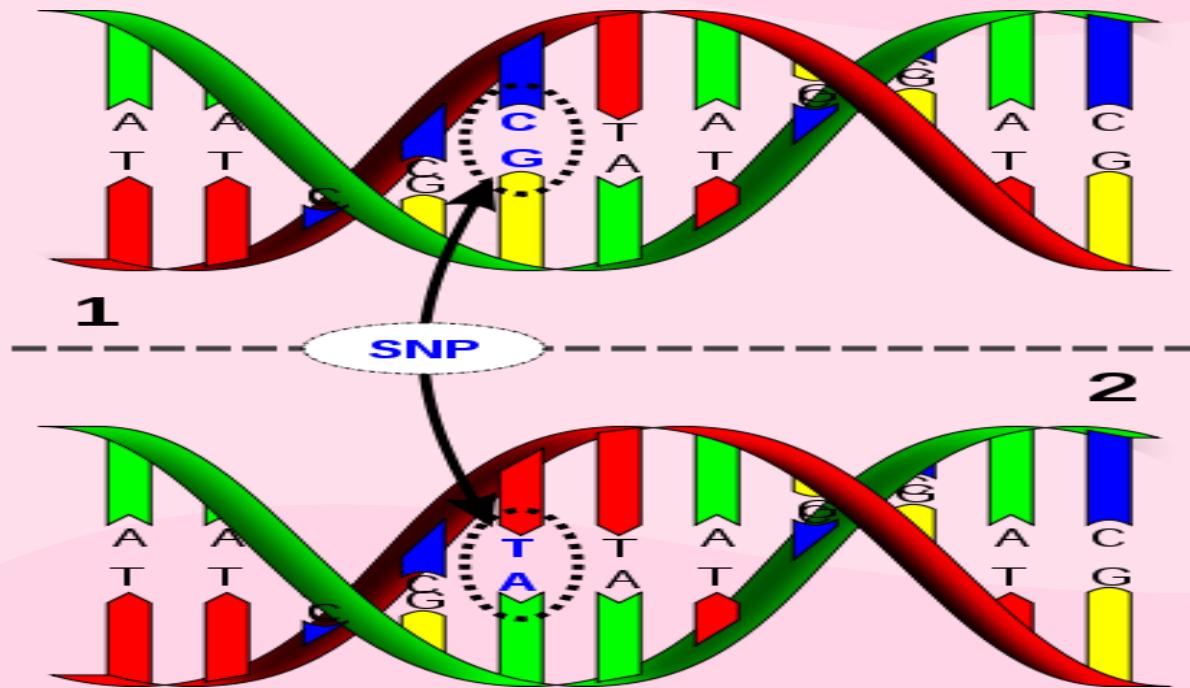
- **Pharmacogenetics** is the study of how individual genetic differences affect drug responses.
- It may enable us to treat the right patient with the right medicine at the right time and at a right dose .

Genetic Polymorphisms

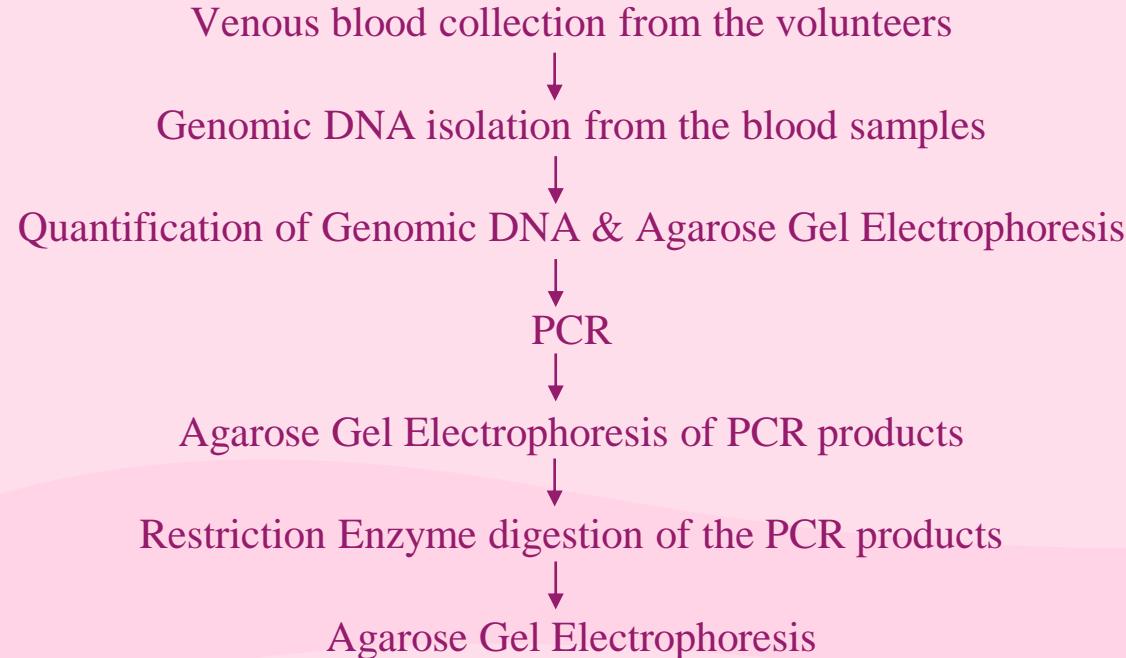
A genetic polymorphism is defined as a deoxyribonucleic acid (DNA) sequence variant.

- Single nucleotide polymorphisms (SNPs)
- Insertions and deletions (indels)
- Variable number tandem repeats (VNTRs) and
- Microsatellites.

SNP (Single Nucleotide Polymorphisms)



Method: Genotyping Subjects



Quantification of Genomic DNA

- The quantity and purity of DNA isolated from blood samples were assessed by using a UV Spectrophotometer (Shimadzu UV Prove v2.1) at 260 nm and at 280 nm.

$$\text{DNA Concentration } (\mu\text{g}/\mu\text{l}) = \frac{\text{OD } 260 \times 50 \text{ (dilution factor)} \times 50 \text{ } \mu\text{g/ml}}{1000}$$

- OD(260)/OD(280) should be=1.7-1.9. (OD= Optical density).
- The purity and integrity of isolated genomic DNA were also assessed by means of Agarose Gel Electrophoresis.

PCR Parameter

Components calculation for PCR stock solution (For 1 Sample):

PCR Solution	Amount (Total 20µl)
Master Mix (Taq DNA Polymerase, dNTP, Reaction Buffer, MgCl2)	10 µl
Forward Primer (Diluted)	1 µl
Reverse Primer (Diluted)	1 µl
Nuclease Free Water	2 µL
Target DNA	6 µl

PCR Condition

Alleles	PCR Conditions		PCR Product Size (bp)
XRCC1 Rs1799782	Cycle	35	485
	Pre Heat	95°C, 5 Minutes	
	Denaturation	95°C, 30 Seconds	
	Annealing	62.5°C, 30 Seconds	
	Extension	72°C, 29 Seconds	
	Final Extension	72°C, 5 Minutes	

Primer Design

Allele	Primer Sequence	M.T. (°C)	Size (bp)
Rs1799782 Forward Primer	GCCAGGGCCCCCTCCTTCAA	69.0	19
Rs1799782 Reverse Primer	TACCCTCAGACCCACGAGT	58.1	19

Restriction Enzyme Digestion

Gene	Enzyme	Digestion Conditions	Expected Fragments (Bp)
XRCC1 Rs19799782	PVU II	Incubation: 37°C for 24 Hours	NH: 485
		Heat Inactivation: 70°C for 15 Minutes	HE: 485, 396, 89
			MH: 396, 89

NH = Normal Homozygote, HE = Mutant Heterozygote, MH = Mutant Homozygote

PCR-RFLP of XRCC1 (rs1799782)

GCCAGGGCCCCCTCCTCAA CATGGGTGTTCATGAGAGGGAAGGAGGCCAGGAAGAGGTTT
CCCTGAGTGAAAAGGGTCTTGGGCCTGGNCTCTGTCCTGGGCCAGACTCCCTGACTCCC
ACCCCTCCTTCCCAGGACTCCCCCTTGGCTTGAGTTGTACGGTTCATAGCCCCCAG
ACAAAGATGAGGCAGAGGCCCGTCCCAGGTAAGCTGTACCTGTCACTCCCCATGGCCTTC
TCCCTGCCTCTCCACCCCCACCTGCCAGCAGCCCACCTATAATACTGACCTTGCAGGACCTT
AGAAGGTGACAGTGACCAAGCTTGGCCAGTTCCGTGTGAAGGAGGAGGATGAGAGGCCA
ACTCTCTGAGGCCGGGGCTCTCTTCAGCCGGATCAACAAGACATCCCCAGGTGAGCT
CGGACAACGTGGGTCTGAGTGAGTAGGGTTGAGACCTAGACTCGTGGGTCTGAGGGTA

Red Targeted SNP (N = C/T)

Green Forward Primer

Yellow Antisense of Reverse Primer

Expected results for XRCC1 (rs1799782)

Genes	REs	Recognition Site	Source
XRCC1 Rs1799782	PVU II	5'...CAG CTG...3' 3'...GTC GAC...5'	Takara Bio Inc, Shiga, Japan
Changes		Fragments	Type
When N=C in both chromosomes (C/C)		485	Normal Homozygote (NH)
When N=C in one chromosome (C/T)		485, 396, 89	Mutant Homozygote (HE)
When N=T in both chromosomes (T/T)		89	Mutant Homozygote (MH)

Digestion of XRCC1 (rs1799782)

WHEN N=C in Both Chromosomes (C/C)

There will be no cutting site for both the chromosomes. So, there will be one fragment (485) for each chromosome.

GCCAGGGCCCCTCCTAACATGGGTGTTCATGAGAGGGAAAGGAAGGCCAGGAAGAGGTTTC
CCTGAGTGAAAAGGGTCTGGGCCCTGG**C**CTCTGTCCTGGGCCAGACTCCCTGACTCCCA
CCCCTCCTTCCCAGGACTCCCCCTTGGCTTGAGTTTGTACGGTTCATAGCCCCCAGA
CAAAGATGAGGCAGAGGCCCGTCCCAGGTAAGCTGTACCTGTCACTCCCCATGGCCTTCT
CCCTGCCTCTCCACCCCCACCTGCCAGCAGCCCACCTATAATACTGACCTTGCAGGACCTT
AGAAGGTGACAGTGACCAAGCTTGGCCAGTTCCGTGTGAAGGAGGAGGATGAGAGCGCCA
ACTCTCTGAGGCCGGGGCTCTCTTCAGCCGGATCAACAAGACATCCCCAGGTGAGCT
CGGACAACGTGGGTCTGAGTGAGTAGGGTTGAGACCTAGACTCGTGGGTCTGAGGGTA

(Fragment 01 = 485 bp)

Digestion of XRCC1 (rs1799782)

WHEN N=C in One Chromosome (C/T)

There is one cutting site for one chromosome (N=T), but for another chromosome (N=C) there is no cutting site. So, there will be three fragments (485, 396, 89) for the two sister chromosomes.

GCCAGGGCCCCCTTCAACATGGGTGTTCATGAGAGGGAAAGGAAGGCCAGGAAGAGGTTTC
CCTGAGTGAAAAGGGTCTTGGGCCCTGGTCTCTGTCCCTGGGCCAGACTCCCTGACTCCCA
CCCCTCCTTCCCAGGACTCCCCCTTGGCTTGAGTTTGTACGGTTCATAGCCCCCCCAGA
CAAAGATGAGGCAGAGGCCCGTCCCAGGTAAGCTGTACCTGTCACTCCCCATGGCCTTCT
CCCTGCCTCTCCACCCCCACCTGCCAGCAGCCCACCTATAATACTGACCTTGCGGGACCTT
AGAAGGTGACAGTGACCAAGCTTGGCCAGTTCCGTGTGAAGGGAGGAGGATGAGAGGCCA
ACTCTCTGAGGCCGGGGCTCTTCTTCAG (**Fragment 01 = 396 bp**)

Digestion of XRCC1 (rs1799782)

CCGGATCAACAAGACATCCCCAGGTGAGCTCGAACACGTGGGTCTGAGTGAG
TAGGGTTGAGACCTAGACTCGTGGGTCTGAGGGTA (**Fragment 02 = 89 bp**)

GCCAGGGCCCTCCTCAACATGGGTGTTCATGAGAGGAAAGGAGCCAGGAAGAGGTTTC
CCTGAGTGAAAAGGGTCTTGGGCCCTGG**C**CTCTGTCCCTGGGCCAGACTCCCTGACTCCCA
CCCCTCCTTCCCAGGACTCCCCCTTGGCTTGAGTTTGTACGGTTCATAGCCCCCAGA
CAAAGATGAGGCAGAGGCCCGTCCCAGGTAAAGCTGTACCTGTCACTCCCCATGGCCTTCT
CCCTGCCTCTCCACCCCCACCTGCCAGCAGCCCACCTATAATACTGACCTTGCAGGACCTT
AGAAGGTGACAGTGACCAAGCTTGGCCAGTCCGTGTGAAGGGAGGAGGATGAGAGCGCCA
ACTCTCTGAGGCCGGGGCTCTCTTCAGCCGGATCAACAAGACATCCCCAGGTGAGCT
CGGACAACGTGGGTCTGAGTGAGTAGGGTTGAGACCTAGACTCGTGGGTCTGAGGGTA
(Fragment 03 = 485 bp)

Digestion of XRCC1 (rs1799782)

WHEN N=T in Both Chromosomes (T/T)

There will be one cutting between 396 bp in both of the chromosomes and two fragments with 396 and 89 will be obtained.

GCCAGGGCCCCTCAACATGGGTGTTCATGAGAGGGAAGGAGGCCAGGAAGAGGTTCC
 CTGAGTGAAAAGGGCTTGGGCCCTGG**T**CTCTGTCCTGGGCCAGACTCCCTGACTCCCACC
 CCTCCTTCCCAGGACTCCCCCTTGGCTTGAGTTTGACGGTTCATAGCCCCCAGACAA
 AGATGAGGCAGAGGCCCGTCCCAGGTAAGCTGTACCTGTCACTCCCCATGGCCTCTCCCT
 GCCTCTCCACCCCCACCTGCCAGCAGCCACCTATAATACTGACCTGCGGGACCTAGAAG
 GTGACAGTGACCAAGCTTGGCCAGTCCGTGTGAAGGAGGAGGATGAGAGCGCCAATCTC
 TGAGGCCGGGGCTCTTCTTCAG (**Fragment 01 = 396 bp**)

CCGGATCAACAAGACATCCCCAGGTGAGCTGGACACGTGGTCCTGAGTGAG
 TAGGGTTGAGACCTAGACTCGTGGGTCTGAGGGTA (**Fragment 02 = 89 bp**)

Gel Electrophoresis



Figure: Addition of sample for Gel Electrophoresis

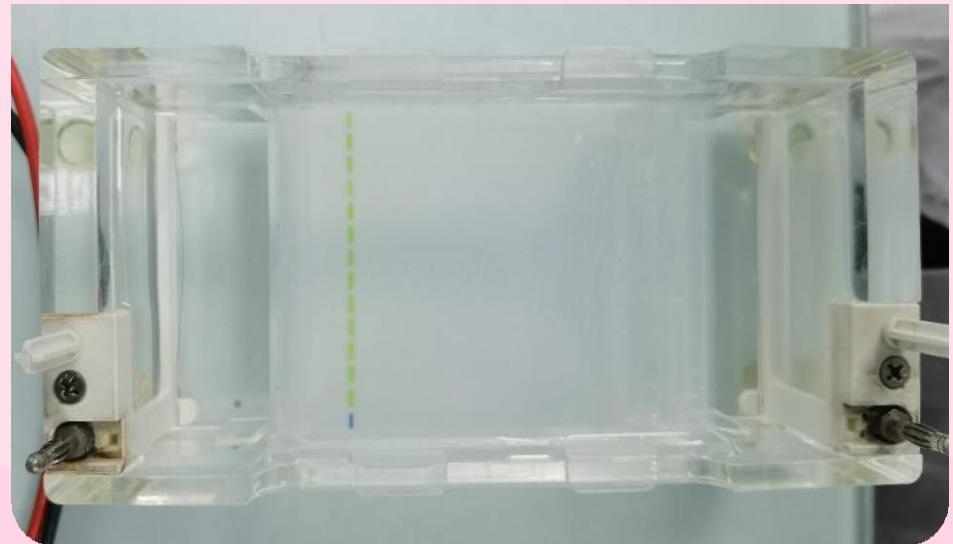
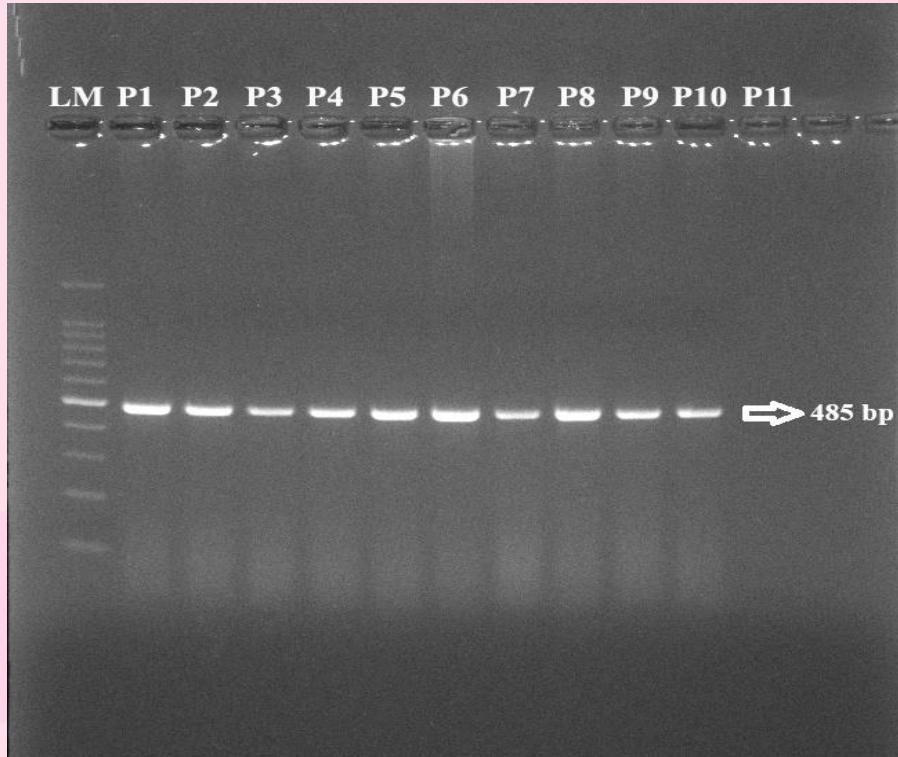


Figure: Gel wells are filled with samples

PCR product of XRCC1 (rs1799782)



Digestion product of XRCC1 (rs1799782)

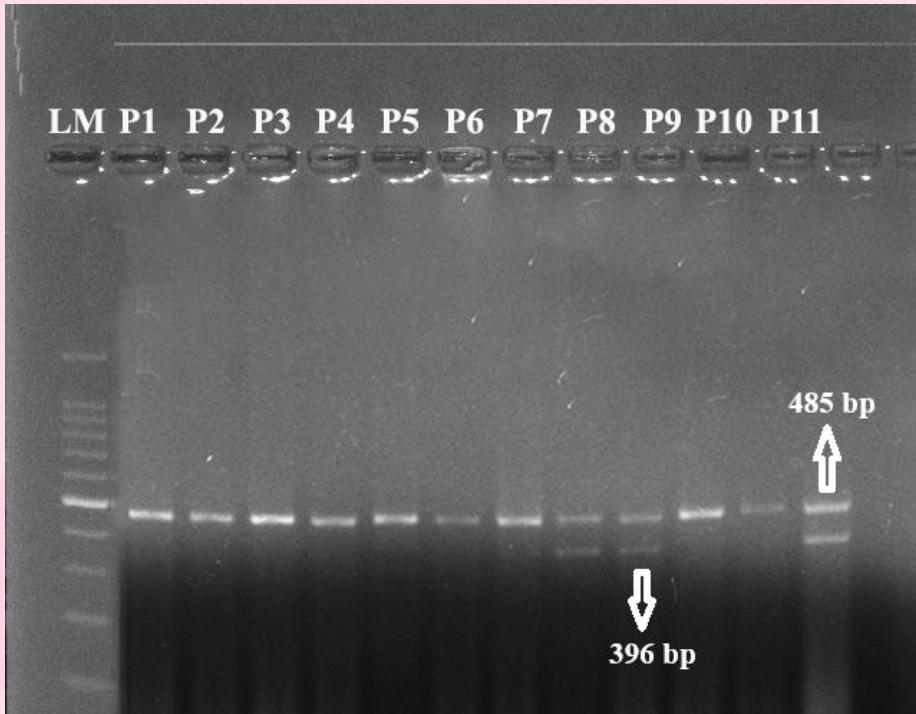


Table 1: Demographic Distributions of the Patients

Demographic Characteristics		Cases (n= 400)
Age		
<45		182
45-55		159
>55		59
45-55 + >55		218
Education		
Under High School		219
At and Over High School		181
Family history of breast cancer in first- and second-degree relatives?		
No		362
Yes		38

Table 1: Demographic Distributions of the Patients

Demographic Characteristics		Cases (n= 400)
Use of Oral Contraceptives		
a. No		154
a. Yes		246
Average Breast Feeding		
a. <12 months		84
a. 12-23 months		169
a. >24 months		147
Area of Residence		
a. Urban		76
a. Sub urban		82
a. Rural		172

Table 2: Statistics of different genotypes

Polymorphisms	Genotype	Cases (n=400)
rs179978982(XRCC1) (C/T)	CC (39%)	156
	CT (40.5%)	162
	TT (20.5%)	82

Table 3: Correlation of XRCC1 gene with clinic-pathological characteristics of the patients

Characteristics	No. of Patients	XRCC1 Carrier(n=41)	XRCC1 Non Carrier (n=359)	OR (95% CI)	P Value
Age (Years)					
<45	182	18	172	Ref.	
45-55	159	17	138	1.1771 (0.5847 to 2.3697)	0.6478
>55	59	6	49	1.1701 (0.4405 to 3.1081)	0.7527
45-55 + >55	218	22	187	1.1242 (0.5831 to 2.1673)	0.7267
Menstrual status					
Premenopausal	172	101	71	Ref	-
Perimenopausal	12	8	4	1.4059 (0.4077 to 4.8489)	0.5896
Postmenopausal	146	96	50	1.3497 (0.8545 to 2.1320)	0.1985

Table 3: Correlation of XRCC1 gene with clinic-pathological characteristics of the patients

Characteristics	No. of Patients	XRCC1 Carrier(n=41)	XRCC1 Non Carrier (n=359)	OR (95% CI)	P Value
TNM stage (Clinical)					
I (Tumor \leq 2 cm)	113	11	109	Ref.	
II (Tumor 2 cm but \leq 5 cm)	142	14	132	1.0510 (0.4585 to 2.4089)	0.9065
III (Tumor 5 cm)	121	13	101	1.2754 (0.5466 to 2.9762)	0.5736
IV (Tumor of any size with direct extension)	24	3	17	1.7487 (0.4421 to 6.9170)	0.4257
Lymph node status					
No (No regional lymph node metastases)	119	11	118	Ref	-
N1 (Metastases to moveable ipsilateral axillary)	184	19	164	1.2428 (0.5701 to 2.7094)	0.5846
N2 (Metastases to fixed ipsilateral axillary lymph nodes)	74	8	60	1.4303 (0.5464 to 3.7441)	0.4660
N3 (Metastases to ipsilateral internal mammary lymph node)	23	3	17	1.8930(0.4790 to 7.4808)	0.3627

Table 3: Correlation of XRCC1 gene with clinic-pathological characteristics of the patients



Characteristics	No. of Patients	XRCC1 Carrier(n=41)	XRCC1 Non Carrier (n=359)	OR (95% CI)	P Value
Histology					
Ductal	387	39	350	Ref.	
Lobular	9	1	6	1.4957 (0.1755 to 12.7477)	0.7127
Mixed	4	1	3	2.9915 (0.3038 to 29.4599)	0.3477
Tumor grade					
Grade I	76	7	75	Ref	-
Grade II	198	20	186	1.1521 0.4677 to 2.8380	0.7583
Grade III	126	14	98	1.5306 (0.5885 to 3.9809)	0.3827

Table 3: Correlation of XRCC1 gene with clinic-pathological characteristics of the patients

Characteristics	No. of Patients	XRCC1 Carrier(n=41)	XRCC1 Non Carrier (n=359)	OR (95% CI)	P Value
Hormone Receptor Status					
Estrogen Receptor(ER)					
Negative	164	17	144	Ref.	-
Positive	236	24	215	0.9456 (0.4906 to 1.8225)	0.8672
Progesterone Receptor(PR)					
Negative	202	21	178	Ref.	-
Positive	198	20	181	0.9366 (0.4907 to 1.7876)	0.8426
Her-2 neu status					
Negative	241	25	207	Ref.	-
Positive	159	16	152	0.8716 (0.4498 to 1.6889)	0.6838

Table 4: Response variation of patients with XRCC1 (rs1799782) polymorphism

XRCC1 (Neoadjuvant: n=182)						
Genotype	Total Responders (106)			Total Non-responders (76)		
	Complete Response (30)	Partial Response(76)	Responders	Stable Condition(73)	Progressive Disease (2)	Non-Responders
CC(70)	8	28	36	33	1	34
CT(75)	12	33	45	29	1	30
TT(37)	10	15	25	12	0	12
CT(75)+ TT(37)	22	49	70	40	1	42

Table 5: Comparison of responders and non responders with XRCC1 (rs1799782) polymorphism

XRCC1 (Neoadjuvant: n=182)				
Genotype	Responders	Non-Responders	Odds Ratio (95 % CI)	P Value
CC(70)	36	34	Ref	-
CT(75)	45	30	1.4167 (0.7336 to 2.7358)	0.2996
TT(37)	25	12	1.9676 (0.8556 to 4.5248)	0.1112
CT(75)+ TT(37)	70	42	1.5741 (0.8595 to 2.8826)	0.1416

Table 6: Anemia in both adjuvant and neoadjuvant chemotherapy

Neoadjuvant: n= 182 + Adjuvant: n=218		XRCC1 (n=400)			
		CC (156)	CT (162)	TT(82)	CT(162)+ TT(82)
Anemia					
Grade >II	224	76	91	57	148
Grade III	115	49	48	18	66
Grade IV	61	31	23	7	30
Grade III(115)+ Grade IV(61)	176	80	71	25	96

Table 7: Comparison of anemia in both adjuvant and neoadjuvant chemotherapy

NA+AD (400)		Anemia			
Gene	Genotype	Grade III(115)+ Grade IV(61)	Grade >II (224)	Odds Ratio	P value
XRCC1 (n=400)	CC (156)	80	76	Reference	-
	CT(162)	71	91	0.7412 (0.4767 to 1.1526)	0.1837
	TT(82)	25	57	0.4167 (0.2367 to 0.7334)	0.0024
	CT(162)+ TT(82)	96	148	0.6162 (0.4107 to 0.9245)	0.0193

Table 8: Neutropenia in both adjuvant and neoadjuvant chemotherapy



Neoadjuvant: n= 182 + Adjuvant: n=218		XRCC1 (n=400)			
		CC (156)	CT (162)	TT(82)	CT(162)+ TT(82)
Neutropenia					
Grade >II	276	98	115	63	178
Grade III	70	37	25	8	33
Grade IV	54	21	22	11	33
Grade III(70)+ Grade IV(54)	124	58	47	19	66

Table 9: Comparison of Neutropenia in both adjuvant and neoadjuvant chemotherapy

NA+AD (400)		Neutropenia			
Gene	Genotype	Grade III(70) + Grade IV(54)	Grade >II (276)	Odds Ratio	P value
XRCC1 (n=400)	CC (156)	58	98	Reference	-
	CT(162)	47	115	0.6906 (0.4317 to 1.1045)	0.1223
	TT(82)	19	63	0.5096 (0.277 to 0.9352)	0.0295
	CT(162)+ TT(82)	66	178	0.6265 (0.4074 to 0.9635)	0.0332

Table 10: Leukopenia in both adjuvant and neoadjuvant chemotherapy



Neoadjuvant: n= 182 + Adjuvant: n=218		XRCC1 (n=400)			
		CC (156)	CT (162)	TT(82)	CT(162)+ TT(82)
Leukopenia					
Grade >II	299	106	126	67	193
Grade III	61	32	21	8	29
Grade IV	40	18	15	7	22
Grade III(61)+ Grade IV(40)	101	50	36	15	51

Table 11: Comparison of Leukopenia in both adjuvant and neoadjuvant chemotherapy

NA+AD (400)		Leukopenia			
Gene	Genotype	Grade III(61) + Grade IV(40)	Grade >II (299)	Odds Ratio	P value
XRCC1 (n=400)	CC (156)	50	106	Reference	-
	CT(162)	36	126	0.6057 (0.3673 to 0.9989)	0.0495
	TT(82)	15	67	0.4746 (0.2470 to 0.9120)	0.0253
	CT(162)+ TT(82)	51	193	0.5602 (0.355 to 0.884)	0.0128

Table 12: Thrombocytopenia in both adjuvant and neoadjuvant chemotherapy

Neoadjuvant: n= 182 + Adjuvant: n=218		XRCC1 (n=400)			
		CC (156)	CT (162)	TT(82)	CT(162)+ TT(82)
Thrombocytopenia					
Grade >II	395	152	161	82	243
Grade III	4	3	1	0	1
Grade IV	1	1	0	0	0
Grade III(4)+ Grade IV(1)	5	4	1	0	1



Table 13: Comparison of Thrombocytopenia in both adjuvant and neoadjuvant chemotherapy

NA+AD (400)		Thrombocytopenia			
Gene	Genotype	Grade III(4) + Grade IV(1)	Grade >II (395)	Odds Ratio	P value
XRCC1 (n=400)	CC (156)	4	152	Reference	-
	CT(162)	1	161	0.2360 (0.0261 to 2.1355)	0.1989
	TT(82)	0	82	0.2054 (0.0109 to 3.8620)	0.2903
	CT(162)+ TT(82)	1	243	0.1564 (0.0173 to 1.4123)	0.0984

Table 14: Gastrointestinal Toxicity in both adjuvant and neoadjuvant chemotherapy

Neoadjuvant: n= 182 + Adjuvant: n=218		XRCC1 (n=400)			
		CC (156)	CT (162)	TT(82)	CT(162)+ TT(82)
Gastrointestinal Toxicity					
Grade >II	348	127	146	75	221
Grade III	49	27	15	7	22
Grade IV	3	2	1	0	1
Grade III(49)+ Grade IV(3)	52	29	16	7	23

Table 15: Comparison of Gastrointestinal Toxicity in both adjuvant and neoadjuvant chemotherapy

NA+AD (400)		Gastrointestinal Toxicity			
Gene	Genotype	Grade III(49) + Grade IV(3)	Grade >II (348)	Odds Ratio	P value
XRCC1 (n=400)	CC (156)	29	127	Reference	-
	CT(162)	16	46	1.5232 (0.7584 to 3.0594)	0.2369
	TT(82)	7	75	0.4087 (0.1707 to 0.9789)	0.0447
	CT(162)+ TT(82)	23	221	0.4558 (0.2529 to 0.8215)	0.0089

Conclusion

The findings of this study is XRCC1 gene is related with chemotherapy included toxicity of anemia, neutropenia, leukopenia, gastrointestinal toxicities. Response variation is not associated the polymorphisms of these genes. No other association with clinicopathological characters or demographic distribution was found in this study.