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Polymorphisms; Tamoxifen; Sulfotransferase

Tamoxifen is commonly used as a hormonal therapy for patients with oestrogen-receptor (ER)-positive breast cancer. e biotransformation of tamoxifen is mediated by cytochrome P450 enzymes mainly through demethylation and hydroxylation to form several primary metabolites, principally 4-OH-tamoxifen, metabolites,
ER with greater a nity [1,2]. Endoxifen has 100-fold greater a nity for the estrogen receptor and is 30 - 100 fold more potent than tamoxifen in suppressing estrogen dependent cell proliferation. Endoxifen is considered an entity responsible for signi cant pharmacologic e ect of tamoxifen. A further step in the metabolism of tamoxifen is sulfate conjugation, catalyzed by members of the sulfotransferase family

All new cases of clinically con rmed breast cancer would be taken for study. Patients of con rmed breast cancer who give their consent were included. All patients who refuse to give consent were excluded.

DNA was isolated from the tissue samples from breast cancer patients and blood samples from healthy volunteers by a rapid non-enzymatic method by salting out cellular proteins with saturated solution and precipitation by dehydration [9]. e red blood cells were lysed completely using RBC lyses solution. e lysate were then treated with cell lysis solution in order to lyse the cell components. e protein content is removed by protein precipitation solution. e precipitated DNA was suspended in 70% ethanol in order to remove the salts. e DNA was then dissolved in TE bu er and stored at 4°C Cell lysis, protein precipitation. DNA precipitation and DNA hydration were carried out in the experiment.

CYP2D6*

Genotyping of *C 2D6*4 gene polymorphism, polymerase chain reaction (PCR) was performed, with speci c primers synthesized from Bioserve Biotechnologies Ltd. (Hyderabad, India): 5'-GCCTTCGCCAACCACTCCG-3' (forward) and 5'-AAATCCTGCTCTTCCGAGGC-3' (reverse). A three-step PCR was standardized using an takarathermocycler and carried out with initial denaturation at 94°C for 5 min, followed by 35 cycles of denaturation at 94°C for 30 s, annealing at 60°C for 30 s, and extension at 72°C for 45s. A nal extension at 72°C for 5 min was carried out. Ampli cation products corresponding to 334bp, respectively, were visualized a er electrophoresis in an ethidium-bromide-stained 2% agarose gel. e ampli ed PCR products were performed RFLP using BstN1(Fermentas) restriction enzyme for 37°C overnight PCR products subjected to enzyme digestion was visualized on 3% agarose gel stained with ethidium bromide (Figures 1 and 2).

SULT1A1*

Genotyping of *S 1A1*2* gene polymorphism, polymerase chain reaction (PCR) was performed, with speci c primers synthesized from Bioserve BioCTTCGCCAACCACTCT*[(synthe*[(syntEMC It 05TTCGCC/Span(GCC/(reaction)5uct%6-c)-4u44T%6-c)GCGT[(5'C

Tables 1 and 2 shows the results of *C 2D6* genotypes, out of 140 tamoxifen treated cases 70% (n=98) cases were extensive metabolizers, 30% (n=42) cases were intermediate extensive metabolizers, and in tamoxifen not treated cases out of 140 cases 85% (n=118) cases were extensive metabolizers, 15% (n=22) cases were intermediate extensive metabolizers, In *S 1A1* genotypes out of 140 cases tamoxifen treated cases, 77.14% (n=108) cases were extensive metabolizers, 22.85% (n=32) cases were intermediate extensive metabolizers, and there were no poor metabolizers cases, and in tamoxifen not treated cases out of 140 cases 81.42% (n=114) cases were extensive metabolizers, 18.57% (n=26) cases were intermediate metabolizers.

CYP2D6*4 SULT1A1

Out of total 140 tamoxifen treated cases 42 cases showed *C 2D6**4 polymorphism, In this we found 21.62% (n=8) cases received the drug for 5 years, 5.40% (n=2) cases received for 4 years, 21, 62% (n=8) cases received for 3 years and 27.07% (n=10) cases were receiving from last 2 years and 16.21% (n=6) cases were receiving from below 1 year. Out of total 140 tamoxifen treated cases 32 cases had *S 1A1* polymorphism, out of these 32 cases 9.90% (n=2) cases were on the drug for 5 years, 18.18% (n=4) cases were on drug for 4 years, 27.27% (n=6) cases received for 3 years, 36.36% (n=8) cases received for 2years, and 9.90% (n=2) cases were receiving from below 1 year perhaps continuing till date. In our study we found 9 recurrence cases with *C 2D6**4 polymorphism, 7 recurrence cases with *S 1A1* polymorphisms, we found 2 were no more a er 5 years of treatment, and in non tamoxifen cases 4 recurrent cases which were showing *C 2D6**4 and *S 1A1**1 polymorphisms and no deaths were reported (Figure 4).

To evaluate the prognostic signi cance of tamoxifen therapy in breast cancer patients, survival study was carried out for 5 years. Out of 140 tamoxifen-treated cases, 42(30%) cases had shown GA polymorphism for *C 2D6* gene. Among these 42 patients, the average

better disease-free survival in patients homozygous for *C 2D6**4.

For *C 3A5*, *S 1A1* and *2B15*