Results tables

Table 1: Baseline Characteristics

|  |  |
| --- | --- |
| Baseline characteristic |  |
| Age (median and range) | 45 years (18-80 years) |
| Ethnicity   1. Hindu 2. Muslim 3. Others | 134 (57.51%)  68 (29.18%)  31 (13.32%) |
| Marital Status   1. Married 2. Unmarried | 225 (95.34%)  11 (4.66%) |
| Education status   1. Illiterate 2. Graduate 3. Post Graduate | 89 (37.87%)  98 (41.70%)  48 (20.43%) |
| Occupation   1. Unemployed 2. Employed | 176 (75%)  59 (25%) |
| Age at Menarche (median and range | 13 years (11-18) |
| Age at 1st child birth | 21.5 years (15-37) |
| Duration of breast feeding (median and range) | 18 months (2-60) |
| History of alcohol consumption | 6 (2.54%) |
| History of oral contraceptive use | 19 (8.05%) |
| History of tubal ligation | 28 (11.86%) |
|  |  |
| Previous history of hysterectomy | 15 (6.35%) |
| Metachronous breast cancer | 5 (2.1%) |
| Significant family history | 34 (14.4%) |
| No of 1st degree relatives (median and range) | 8 (3-16) |
| No of 2nd degree relatives (median and range) | 15 (4-40) |
| Clinical stage  1. Stage I  2. Stage II  3. Stage III  4. Stage IV | 18 (7.63%)  83 (35.16%)  81 (34.32%)  54 (22.88%) |
| Receptor status   1. Hormone positive 2. Triple positive 3. Her2 positive 4. Triple negative | 108 (45.76%)  32 (13.55%)  79 (33.47%)  83 (35.17%) |

Table 2: Prevalence of pathogenic/likely pathogenic mutations in NCCN qualifiers vs non qualifiers

|  |  |
| --- | --- |
| No of patients qualifying NCCN criteria for testing   1. One criteria fulfilled 2. Two criteria fulfilled 3. Three criteria fulfilled 4. Four criteria fulfilled   Which NCCN criteria fulfilled   1. Breast cancer <50 years 2. TNBC <60 years 3. Two breast primaries at any age 4. Positive family history as defined by NCCN (see footnote) | 165 (69.92%)  88 (37.28%)  59 (25%)  16 (6.77%)  2 (0.8%)  151 (91.51%)  69 (41.8%)  5 (3.03%)  34 (20.6%) |
| No of patients not qualifying NCCN criteria | 71 (30.08%) |
| Pathogenic mutations in patients qualifying NCCN criteria | 39 (23.63%) |
| Pathogenic mutations in patients not qualifying NCCN criteria | 5 (7.04%) |
| No of mutations missed if only NCCN qualifiers tested | 5/44= 11.36% |
|  |  |
| No of patients qualifying MCG criteria for testing   1. One criteria fulfilled 2. Two criteria fulfilled 3. Three criteria fulfilled 4. Four criteria fulfilled   Which MCG criteria fulfilled   1. Breast cancer <45 years 2. TNBC at any age 3. Two breast primaries at <60 years of age 4. Positive family history as defined by MCG (see footnote) | 153 (64.83%)  89 (37.71%)  44 (18.64%)  17 (7.2%)  2 (0.8%)  127 (83%)  68 (44.44%)  5 (3.26%)  34 (22.22%) |
| No of patients not qualifying MCG criteria | 83 (35.16%) |
| Pathogenic mutations in patients qualifying MCG criteria | 38 (24.83%) |
| Pathogenic mutations in patients not qualifying MCG criteria | 6 (7.22%) |
| No of mutations missed if only MCG qualifiers tested | 6/44 (13.63%) |

Table 3: Description of mutations (P/LP) (N=44)

|  |  |
| --- | --- |
| BRCA1   * Exon 10 * Exon 16 * Exon 2 * Exon 4 * Exon 17 * exon 6 * intron 15 * intron 12 | 22  10  2  3  2  2  1  1  1  1 |
| BRCA2   * exon 11 * exon 24 * exon 10 * intron 10 * Exon 15 * Exon 3 | 9  4  1  1  1  1  1 |
| PALB2   * exon 3 * exon 7 * exon 4 * exon 5 | 4  1  1  1  1 |
| P53   * exon 10 * exon 6 * exon 7 | 3  1  1  1 |
| ATM   * exon 22 * exon 33 | 2  1  1 |
| FANCI   * Intron 22 * exon 10 | 2  1  1 |
| RAD50   * Exon 23 * Exon 18 | 2  1  1 |
| RAD51d   * Exon 5 | 1 |
| MUTYH   * exon 9 | 1 |
| MSH2   * exon 3 | 1 |

\*Three patients had pathogenic mutations in both BRCA1 and ATM, BRCA1 and FANCI, BRCA2 and ATM respectively

Table 4: Description of mutations (VUS)

|  |  |
| --- | --- |
| ATM | 15 |
| ATR | 2 |
| BARD1 | 2 |
| BLM | 1 |
| BRCA1 | 3 |
| BRCA2 | 9 |
| BRIP1 | 5 |
| CDH1 | 6 |
| CHEK2 | 4 |
| ERCC2 | 2 |
| FANCA | 2 |
| FANCD2 | 2 |
| FANCE | 3 |
| FANCF | 1 |
| FANCI | 1 |
| FANCM | 5 |
| HMMR | 1 |
| MLH1 | 5 |
| MLH3 | 2 |
| MRE11A | 2 |
| MSH2 | 5 |
| MSH3 | 1 |
| MSH6 | 6 |
| MUTYH | 2 |
| NBN | 3 |
| NF1 | 1 |
| NF2 | 1 |
| PMS2 | 6 |
| RAD50 | 7 |
| RAD51D | 3 |
| RAD54L | 11 |
| RECQL4 | 10 |
| RNASEL | 1 |
| SBDS | 1 |
| SDHB | 1 |
| SEC23B | 2 |
| RET | 1 |
| MSR1 | 1 |
| PRF1 | 1 |
| TMEM 127 | 1 |
| TP53 | 3 |
| WRN | 1 |

Table 5: Interventions in patients with pathogenic mutations in BRCA1/2 (N-31)

|  |  |
| --- | --- |
| Risk Reducing Surgery   * RRSO Advised * RRSO done * RRM advised * RRM done | 24 (77.4%)  7 (29.16%)  27 (77.4%)  10 (37.37%) |
| Not advised RRSO  Reasons for not advising RRSO   * metastatic disease * family not complete | 7 (22.58%)  3  4 |
| Not advised RRM  Reasons for not advising RRM   * metastatic disease * Previous B/L mastectomy | 4 (12.9%)  3  1 |
| Reason for not undergoing RRSO  COVID-19 pandemic  Not willing for surgery | 14  3 |
| Family testing | 16/44 (38.63%) |
| Reasons for not doing testing   * not willing for testing * Financial * COVID (post-test not accessible)   Previvors Tested  Report collected  Previvors positive for mutation  Report awaited | 5  17  6  32  26  20  6 |

Table 6: Factors predicting presence of P/LP mutations

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Mutation negative | Mutation positive | P value | Sensitivity | Specificity | PPV | NPV |
| NCCN non qualifier  NCCN qualifiers | 66  126 | 5  39 | 0.03 | 23.6 (17.5-30.9) | 92.9 (83.6-97.4) | 88.6 (74.6-95.7) | 34.4 (27.8-41.6) |
| Individual NCCN criteria  BC>50  BC<50  TNBC>60  TNBC<60  Two breast primaries-No  Two Breast primaries-Yes  No family history  Positive family history | 74  118  146  44  192  0  181  11 | 11  33  19  25  39  5  23  21 | 0.118  <0.001  <0.001  <0.001 | 21.8 (15.7-29.4)  36.2 (25.2-48.7)  100 (46.3-100)  65.6 (46.8-80.8) | 87.1 (77.6-93.1)  88.5 (82.4-92.8)  83.1 (77.5-87.6)  88.7 (83.4-92.6) | 75 (59.4-86.3)  56.8 (41.1-71.3)  11.4 (4.3-25.4)  47.7 (32.7-63.1) | 38.5 (31.7-45.9)  76.8 (70.1-82.5)  100 (97.6-100)  94.3 (89.7-97) |
| MCG non qualifier  MCG qualifier | 75  115 | 6  38 | 0.001 | 24.8 (18.4-32.6) | 92.6 (84-96.6) | 86.4 (72-94.3) | 39.5 (32.5-46.8) |
| Individual MCG  BC>45  BC<45  TNBC any age-no  TNBC any age-yes  Two breast primaries <60-no  Two breast primaries <60-yes  No family history  Positive family history | 94  96  146  44  192  0  181  11 | 13  31  20  24  39  5  23  21 | 0.012  <0.001  <0.001  <0.001 | 24.4 (17.4-33)  35.3 (24.4-47.9)  100 (46.3-100)  65.6 (46.8-80.8) | 87.9 (79.8-93.1)  88 (81.8-92.3)  83.1(77.5-87.6)  88.7(83.4-92.6) | 70.5 (54.6-82.8)  54.5 (39-69.3)  11.4 (4.3-25.4)  47.7 (32.7-63.1) | 49.5 (42.2-56.8)  76.8 (70.1-82.5)  100 (97.6-100)  94.3 (89.7-97) |
| ER/PR neg  ER/PR positive | 99  91 | 28  16 | 0.18 | 23.5 (16.4-32.4) | 86.1 (78.1-91.6) | 63.6 (47.7-77.2) | 52.1 (44.8-59.4) |
| Her2 neg  Her2 pos | 119  71 | 37  7 | 0.007 | 23.7 (17.4-31.3) | 91 (81.9-96) | 84.1 (69.3-92.8) | 37.4 (30.6-44.7) |

Table 7:

|  |  |
| --- | --- |
| **VUS characterisation** | **Number (%)** |
| No of patients with VUS only | 89 (37.71%) |
| No of patients with P/LP Plus VUS | 21 (8.89%) |
| Total patients harboring a VUS | 110 (46.61%) |
| Total no of VUS mutations | 142 |
| VUS in High penetrance genes (BRCA1, BRCA2, CDH1, P53) | 21 |
| VUS in moderate penetrance genes (ATM, BRIP1, CHEK2, PALB2, RAD) | 45 |

Table 8: Predictors of VUS

|  |  |  |  |
| --- | --- | --- | --- |
|  | VUS negative | VUS positive | P value |
| NCCN non qualifier  NCCN qualifiers | 39  108 | 32  57 | 0.14 |
| Individual NCCN criteria  BC>50  BC<50  TNBC>60  TNBC<60  Two breast primaries-No  Two Breast primaries-Yes  No family history  Positive family history | 51  96  101  46  142  5  120  27 | 34  55  66  23  89  0  84  5 | 0.34  0.461  0.16  0.006 |
| MCG non qualifier  MCG qualifier | 48  99 | 35  54 | 0.326 |
| Individual MCG criteria  BC>45  BC<45  TNBC any age-no  TNBC any age-yes  Two breast primaries <60-no  Two breast primaries <60-yes  No family history  Positive family history | 67  80  101  46  142  5  120  27 | 42  47  67  22  89  0  84  5 | 0.893  0.302  0.16  0.006 |
| ER/PR neg  ER/PR positive | 79  68 | 49  40 | 0.89 |
| Her2 neg  Her2 pos | 106  41 | 51  38 | 0.023 |

Table 9: DAS and IES score (N-223)

|  |  |
| --- | --- |
| Mean DAS Score | 14.1 (0-72) |
| Mean IES Score | 15.66 (2-51) |
| DAS breakdown  Distress  None  Mild  Moderate  Severe  Extremely severe  Anxiety  None  Mild  Moderate  Severe  Extremely severe  Stress  None  Mild  Moderate  Severe  Extremely severe | 73 (32.73)  66 (29.59)  51 (22.86)  7 (3.13)  26 (11.65)  49 (21.97)  25 (11.21)  97 (43.49)  18 (8.07)  34 (15.24)  160 (71.74)  28 (12.55)  8 (3.58)  9 (4.03)  18 (8.07) |
| IES breakdown  No risk  Mild risk  Moderate risk  Severe risk | 178 (79.82)  26 (11.65)  12 (5.38)  7 (3.13) |
| Severe Distress  Severe Anxiety  Severe Stress  Any risk of PTSD | 33 (14.78)  52 (23.31)  27 (12.1)  45 (20.17) |

Table 10: Predictors of severe distress, anxiety, stress and any PTSD

1. Predictors of severe distress

|  |  |  |  |
| --- | --- | --- | --- |
|  | Severe distress - | Severe Distress + | P value |
| Employment  Unemployed  employed | 149  40 | 17  16 | 0.001 |
| Education status  Illiterate  literate | 77  112 | 4  29 | 0.002 |
| Marital status  Married  Unmarried | 182  8 | 31  2 | 0.635 |
| History of Alcohol  negative  positive | 183  6 | 33  0 | 0.299 |
| History of OCP  Negative  Positive | 171  14 | 28  5 | 0.155 |
| History of tubal ligation  Negative  Positive | 158  25 | 29  3 | 0.506 |
| Menarche age  <=13 years  >13 years | 147  43 | 27  6 | 0.569 |
| Age at 1st child birth  <=21  >21 | 72  107 | 7  24 | 0.061 |
| Duration of breast feeding  <=12 months  >12 months | 86  99 | 17  16 | 0.594 |
| NCCN not qualifier  NCCN qualifier | 63  127 | 7  26 | 0.172 |
| BC>50  BC<50 | 74  116 | 10  23 | 0.344 |
| TNBC>60  TNBC<60 | 138  52 | 20  13 | 0.161 |
| Two breast primaries-No  Two Breast primaries-Yes | 188  2 | 30  3 | 0.004 |
| No family history  Positive family history | 171  19 | 21  12 | <0.001 |
| MCG non qualifier  MCG qualifier | 71  119 | 10  23 | 0.436 |
| BC>45  BC<45 | 90  100 | 14  19 | 0.599 |
| TNBC any age-no  TNBC any age-yes | 124  66 | 21  12 | 0.856 |
| P/LP- No  P/LP yes | 154  34 | 23  10 | 0.105 |
| VUS- No  VUS- yes | 116  74 | 23  10 | 0.344 |

1. Predictors of severe anxiety

|  |  |  |  |
| --- | --- | --- | --- |
|  | Severe anxiety - | Severe anxiety + | P value |
| Employment  Unemployed  employed | 139  31 | 27  25 | <0.001 |
| Education status  Illiterate  literate | 77  112 | 4  29 | 0.002 |
| Marital status  Married  Unmarried | 163  8 | 50  2 | 0.8 |
| History of Alcohol  Negative  Positive | 183  6 | 33  0 | 0.299 |
| History of OCP  Negative  Positive | 155  12 | 44  7 | 0.147 |
| History of tubal ligation  Negative  Positive | 143  23 | 44  5 | 0.505 |
| Menarche age  <=13 years  >13 years | 132  42 | 39  10 | 0.569 |
| Age at 1st child birth  <=21  >21 | 66  94 | 13  37 | 0.052 |
| Duration of breast feeding  <=12 months  >12 months | 78  88 | 25  27 | 0.891 |
| NCCN not qualifier  NCCN qualifier | 58  113 | 12  40 | 0.14 |
| BC>50  BC<50 | 68  103 | 16  36 | 0.241 |
| TNBC>60  TNBC<60 | 127  44 | 31  21 | 0.042 |
| Two breast primaries-No  Two Breast primaries-Yes | 169  2 | 49  3 | 0.05 |
| No family history  Positive family history | 157  14 | 35  17 | <0.001 |
| MCG non qualifier  MCG qualifier | 66  105 | 15  37 | 0.2 |
| BC>45  BC<45 | 81  90 | 23  29 | 0.69 |
| TNBC any age-no  TNBC any age-yes | 114  57 | 31  21 | 0.35 |
| P/LP- No  P/LP yes | 138  31 | 39  13 | 0.293 |
| VUS- No  VUS- yes | 106  65 | 33  19 | 0.848 |

1. Predictors of Severe Stress

|  |  |  |  |
| --- | --- | --- | --- |
|  | Severe stress - | Severe stress + | P value |
| Employment  Unemployed  employed | 152  43 | 14  13 | 0.003 |
| Education status  Illiterate  literate | 77  118 | 4  12 | 0.008 |
| Marital status  Married  Unmarried | 188  8 | 25  2 | 0.434 |
| History of Alcohol  Negative  Positive | 189  6 | 27  0 | 0.355 |
| History of OCP  Negative  Positive | 177  14 | 22  5 | 0.054 |
| History of tubal ligation  Negative  Positive | 163  26 | 24  2 | 0.389 |
| Menarche age  <=13 years  >13 years | 151  45 | 23  4 | 0.338 |
| Age at 1st child birth  <=21  >21 | 73  112 | 6  19 | 0.134 |
| Duration of breast feeding  <=12 months  >12 months | 90  101 | 13  14 | 0.92 |
| NCCN not qualifier  NCCN qualifier | 65  131 | 5  22 | 0.124 |
| BC>50  BC<50 | 76  120 | 8  19 | 0.358 |
| TNBC>60  TNBC<60 | 141  55 | 17  10 | 0.336 |
| Two breast primaries-No  Two Breast primaries-Yes | 193  3 | 25  2 | 0.053 |
| No family history  Positive family history | 175  21 | 17  10 | <0.001 |
| MCG non qualifier  MCG qualifier | 73  123 | 8  19 | 0.436 |
| BC>45  BC<45 | 92  104 | 12  15 | 0.599 |
| TNBC any age-no  TNBC any age-yes | 127  69 | 18  9 | 0.848 |
| P/LP- No  P/LP yes | 138  31 | 39  13 | 0.293 |
| VUS- No  VUS- yes | 119  77 | 20  7 | 0.179 |

1. Predictors of any PTSD (IES)

|  |  |  |  |
| --- | --- | --- | --- |
|  | PTSD - | PTSD + | P value |
| Employment  Unemployed  employed | 147  30 | 19  26 | <0.001 |
| Education status  Illiterate  literate | 76  101 | 5  40 | <0.001 |
| Marital status  Married  Unmarried | 171  7 | 42  3 | 0.429 |
| History of Alcohol  Negative  positive | 173  5 | 43  1 | 0.844 |
| History of OCP  Negative  Positive | 164  12 | 35  7 | 0.042 |
| History of tubal ligation  Negative  Positive | 150  24 | 37  4 | 0.49 |
| Menarche age  <=13 years  >13 years | 139  39 | 35  10 | 0.964 |
| Age at 1st child birth  <=21  >21 | 69  99 | 10  32 | 0.039 |
| Duration of breast feeding  <=12 months  >12 months | 82  91 | 21  24 | 0.93 |
| NCCN not qualifier  NCCN qualifier | 59  119 | 11  34 | 0.261 |
| BC>50  BC<50 | 69  109 | 15  30 | 0.502 |
| TNBC>60  TNBC<60 | 130  48 | 28  17 | 0.154 |
| Two breast primaries-No  Two Breast primaries-Yes | 175  3 | 43  2 | 0.264 |
| No family history  Positive family history | 160  18 | 32  13 | 0.001 |
| MCG non qualifier  MCG qualifier | 67  111 | 14  31 | 0.416 |
| BC>45  BC<45 | 85  93 | 19  26 | 0.506 |
| TNBC any age-no  TNBC any age-yes | 117  61 | 28  17 | 0.659 |
| P/LP- No  P/LP yes | 142  34 | 35  10 | 0.663 |
| VUS- No  VUS- yes | 108  70 | 31  14 | 0.31 |

Table 11: Performance of Can risk Score (Based on cut off >10%)

1. for BRCA1

|  |  |  |  |
| --- | --- | --- | --- |
|  | BRCA1+ | BRCA1- | Total |
| CR+ | 12 | 22 | 34 |
| CR- | 10 | 192 | 202 |
| Total | 22 | 214 | 236 |

Sensitivity= 35.3 (20.3-53.5)

Specificity= 95 (90.8-97.5)

PPV= 54.5 (32.7-74.9)

NPV=89.7 (84.7-93.3)

1. for BRCA2

|  |  |  |  |
| --- | --- | --- | --- |
|  | BRCA2+ | BRCA2- | Total |
| CR+ | 2 | 10 | 12 |
| CR- | 7 | 217 | 224 |
| Total | 9 | 227 | 236 |

Sensitivity= 16.7(2.9-49.1)

Specificity= 97 (93.6-98.7)

PPV= 22.2 (3.9-59.8)

NPV=95.7 (92-97.8)

1. for any BRCA

|  |  |  |  |
| --- | --- | --- | --- |
|  | Any BRCA+ | Any BRCA- | Total |
| CR+ | 19 | 33 | 52 |
| CR- | 12 | 172 | 184 |
| Total | 31 | 205 | 236 |

Sensitivity= 36.5(23.9-51.1)

Specificity= 93.5 (88.6-96.4)

PPV= 61.2 (42.3-77.6)

NPV=83.9 (78-88.5)

1. for any genes

|  |  |  |  |
| --- | --- | --- | --- |
|  | Any genes+ | Any genes- | Total |
| CR+ | 27 | 58 | 85 |
| CR- | 17 | 134 | 151 |
| Total | 44 | 192 | 236 |

Sensitivity= 31.8(22.3-42.9)

Specificity= 88.7 (82.3-93.1)

PPV= 61.4 (45.5-75.3)

NPV=69.8 (62.7-76.1)

Table 12: Performance of MYRIAD score

|  |  |  |  |
| --- | --- | --- | --- |
|  | Any BRCA+ | Any BRCA- | Total |
| Myriad+ | 13 | 11 | 24 |
| Myriad- | 18 | 194 | 212 |
| Total | 31 | 205 | 236 |

Sensitivity= 54.16 (33.2-73.8)

Specificity= 91.5 (86.7-94.7)

PPV= 41.9 (25.1-60.7)

NPV=94.6 (90.3-97.1)

Table 13: Performance of PENN score

|  |  |  |  |
| --- | --- | --- | --- |
|  | Any BRCA+ | Any BRCA- | Total |
| PENN+ | 25 | 81 | 106 |
| PENN- | 6 | 124 | 130 |
| Total | 31 | 205 | 236 |

Sensitivity= 23.6 (16.1-33)

Specificity= 95.4(89.8-98.1)

PPV= 80.6 (61.9-91.9)

NPV=60.5 (53.4-67.2)

* ROC of all the scores