ABSTRACT... Objectives: The aim of our study is to compare the efficacies of Pap smear cytology, colposcopy and histopathology, in diagnosis of cervical diseases. Study Design: Cross sectional cohort study. Period: One year from June 2013 to June 2014. Setting: Tertiary care hospital in Karachi, Pakistan. Method: The patient population n=145 consisted of women ranging from age 18 to 80 years old, who had come to the outpatient clinics for a variety of symptoms. Pap smear, colposcopy and histopathology was done for women who had symptoms like recurrent vaginal discharge, postcoital bleeding and other diseases of the cervix. Findings were noted on a proforma and all the patients signed a duly informed consent. Data was analyzed using SPSS version 23. Results: The mean age was 45 +/- 9 years (between 24 – 75 years), the parity was 5 +/- 4, normal colposcopy findings were found in n= 66 women, while abnormal findings were found in n=79 women. In the abnormal colposcopic finding group n=63 had abnormal histopathology (p<0.001) abnormal histopathology was found in n=11 women who had normal colposcopic findings (16.67% false negative), the calculated sensitivity and specificity of colposcopy was determined to be 86% and 79%. For pap smear abnormality was found in n= 49 patients, out of which n=29 had abnormal findings on histopathology as well. And for colposcopy and pap smear out of n= 78 patients who had abnormal colposcopic findings, abnormal pap smear was found in only n= 28 patients. And out of those who had normal colposcopy n= 67, n= 21 had abnormal pap smear (False positivity of 31.34%) similarly out of those who had normal pap smear n= 96, n= 44 had abnormal histopathology (false negativity of 45.83%). The calculated sensitivity and specificity of pap smear was 38.8% and 71.8% respectively. Conclusion: We have concluded that there is a strong correlation between findings of colposcopy and histopathological diagnosis, but when it comes to the diagnosis made by pap smear and colposcopy and pap smear and histopathology the correlation is weak and not consistent.

Key words: Pap smear, colposcopy, histopathology, cervix, correlation, cancer.
developing countries cytology is not used due to lack of access and economical issues, and also cytology alone is not a successful screening tool to identify women with preneoplastic lesions, hence a lot of patients are being missed. Colposcopy is also a viable method that is used in cancer prevention, and it helps to diagnose the pre-cancerous lesions and allow women to be get effective treatment as based on the stage of their disease, but colposcopy is also being questioned for accuracy as cases have been reported where loop excision studies diagnosed CIN 2 and above, while colposcopy failed to recognize such lesions. The aim of our study is to compare the efficacies of pap smear cytology, colposcopy and histopathology and find the correlations and agreements between their respective findings for the diagnosis of cervical cancer or pre-cancerous lesions of the cervix and associated parts of the female anatomy.

MATERIALS AND METHODS
The type of study is a cross sectional cohort study, done for a period of one year from June 2013 to June 2014 at a tertiary care hospital in Karachi, Pakistan. The patient population consisted of women ranging from age 18 to 80 years old, who had come to the out patient clinics for a variety of symptoms. Pap smear, colposcopy and histopathology was done for women who had symptoms like recurrent vaginal discharge, postcoital bleeding and other diseases of the cervix. Patients already diagnosed as cases of cervical cancer or treated for it were excluded from the study. The sample size was calculated using power analysis and sample size software based on different techniques as described in studies, the sample size was calculated to be n=145. Findings were noted on a proforma (colposcopy findings, cytology and histopathology reports). Abnormal cytology included ASCUS, LSILS, HSILS and invasive carcinoma. Presence of aceto white areas and abnormal vasculature in and around the cervix was considered an abnormal finding on the colposcopy examination, biopsy samples were obtained for histopathological analysis. The classification was as CIN 1,2,3 normal and invasive carcinoma. All the patients signed a duly informed consent. Chi square test was used for the assessment of significance of association. The analysis for agreement was done between cytology and histopathology, colposcopy and cytology, colposcopy and histopathology. Data was analyzed using SPSS version 23.

RESULTS
The total study population consisted of n=145 women, whose mean age was 45 +/- 9 years (between 24 – 75 years), the parity was 5 +/- 4, normal colposcopy findings were found in n=66 women, while abnormal findings were found in n=79 women. In the abnormal colposcopic finding group n=63 had abnormal histopathology (p<0.001) abnormal histopathology was found in n=11 women who had normal colposcopic findings (16.67% false negative), the calculated sensitivity and specificity of colposcopy was determined to be 86% and 79%.

<table>
<thead>
<tr>
<th>Colposcopy</th>
<th>Abnormal Histopathology</th>
<th>Normal Histopathology</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>63 (79.75%)</td>
<td>16 (20.25%)</td>
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<td>11 (16.67%)</td>
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<table>
<thead>
<tr>
<th>Colposcopy</th>
<th>Abnormal Pap smear</th>
<th>Normal Pap smear</th>
<th>p-value</th>
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<tbody>
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<td>21 (31.34%)</td>
<td>46 (68.66%)</td>
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<table>
<thead>
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<th>Pap smear</th>
<th>Abnormal Histopathology</th>
<th>Normal Histopathology</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>29 (59.18%)</td>
<td>20 (40.82%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Normal</td>
<td>44 (45.83%)</td>
<td>52 (54.17%)</td>
<td></td>
</tr>
</tbody>
</table>

Table. Comparison of Colposcopy, histopathology and pap smear.
For pap smear abnormality was found in n= 49 patients, out of which n=29 had abnormal findings on histopathology as well. And for colposcopy and pap smear out of n= 78 patients who had abnormal colposcopic findings, abnormal pap smear was found in only n= 28 patients. And out of those who had normal colposcopy n= 67, n= 21 had abnormal pap smear (False positivity of 31.34%) similarly out of those who had normal pap smear n= 96, n= 44 had abnormal histopathology (false negativity of 45.83%). The calculated sensitivity and specificity of pap smear was 38.8% and 71.8% respectively. Refer to Table-I.

DISCUSSION
A good percentage of high grade lesions are not detected by pap smear, due to its well recognized limitations. According to various studies there exists a variation among the various parameters of the pap smear such as its accuracy, specificity and sensitivity. In our study we found that out of the n=44 normal pap smear, n=73 had abnormalities as observed by histopathological analysis, like wise when it came to colposcopy n=78 had abnormal findings while among the group n=50 had normal pap smear, so a significant agreement was not determined between pap smear as compared with colposcopy or histopathology. According to a study the correlation of cytology and histology was found to be 77.5% when it comes to high grade lesions, and in a retrospective review it was found that the accuracy of cytology was 62.7%. A massive systemic review that comprised of meta analysis of 94 studies, sought to determine the accuracy of the pap test for screening and surveillance of cytological abnormalities, and concluded that the studies had biases, and the best studies were able to show only moderate agreement when it comes to high accuracy, it possessed a sensitivity which ranged between 30 and 70% and specificity which ranged between 86 to a 100%. Another meta analysis concluded that sensitivity and specificity for cytology when it comes to high grade lesions is between 55.2 and 75.6% and for low grade lesions is found to be between 81 and 96.7% respectively. A prospective study of India of 2008 shows that there is a lack of agreement between cytology and histopathology and it concludes that in patients who have persistent inflammatory pap smear can have cervical intraepithelial neoplasia, according to a study there was agreement between pap smear and cervical biopsy ( k=0.5 ) and another study concluded that a high agreement between cytology and histopathology exists of 82%, but it comprised mainly of patients having low grade intraepithelial lesions.

According to a prospective study which evaluated the agreement between colposcopy and histopathology, it was found that there exists an agreement between the two afore mentioned variables and it is a significant relationship, the negative predictive value of a benign lesion as observed by colposcopy was found to be 70.5%, its sensitivity and specificity were 74% and 90.7% respectively, a similar study also showed the same agreement ( k= 0.66 ). While according to a study the association was significant but the strength of agreement was poor ( k=0.20). A study done to find out the accuracy of the grading done using colposcopy of high grade cervical intraepithelial neoplasia shows that the observation of aceto white lesions identified CIN2+ and biopsy maximizes the sensitivity and specificity of the diagnosis.8 A study done in India concluded that the sensitivity and specificity of colposcopy when it comes to the detection of CIN is 74.7% and 92.9% respectively. In our study the findings of colposcopy were found to be normal in cases of patients who had abnormal histopathology, which comes out to be a specificity of 79%. And it is concluded that colposcopy helps in indentifying the best site for obtaining a sample for histopathological analysis and for the diagnosis of intraepithelial neoplasia. According to a study colposcopy with biopsy is successful in detection of two third cases of CIN III and has a greater sensitivity when multiple biopsies are performed. Which is also consistent with an another study which found that multiple biopsies increase the accuracy. According to a meta-analysis of eight studies, there is a high accuracy of colposcopy (89%) with a concordance rate to be found in 61% of cases, when the results are compared with histopathological findings,
but they also found an equal number of false positives and false negatives. In our study the abnormal colposcopic findings showed good concordance to histopathological analysis which is also similar to the results of a recent study, as compared to the concordance of pap smear with colposcopic findings which had a poor concordance, which is also observed in a similar study. And the agreement between cytology and histopathology was found to be of moderate significance, which is also shown in the study. Thus it is concluded that colposcopy not only helps in determination of the best place for biopsy it also helps in the diagnosis of CIN. A sensitivity of 90.2% and specificity of 48.6% was found in a study that compared the inter observer variability of colposcopy when it comes to the diagnosis of CIN according to the histopathological results.

CONCLUSION
We have concluded that there is a strong correlation between findings of colposcopy and histopathological diagnosis, but when it comes to the diagnosis made by pap smear and colposcopy and pap smear and histopathology the correlation is weak and not consistent.

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