Cyclooxygenase-2 (COX-2) is a prostaglandin synthase that catalyzes the synthesis of prostaglandin G2 and H2. It has been shown that COX-2 plays an important role in tumorigenesis of different tumor types and it is thought to take part in breast carcinogenesis. In the present study, we aimed to investigate the relationship of immunohistochemical COX-2 expression with clinicopathological parameters, including HER-2/neu overexpression in invasive breast carcinoma (IBC). Our study population comprised 10 normal breasts, 25 ductal carcinomas in situ (DCIS), and 51 invasive breast carcinomas. Immunohistochemical overexpressions of COX-2 and HER-2/neu were investigated in sections of formalin-fixed, paraffin-embedded blocks by 3 observers. In normal breast, DCIS and IBC, the COX-2 overexpression rate was 0%, 84%, and 58.8%, respectively. In IBC, COX-2 overexpression had a significant relationship with HER-2/neu overexpression (p=0.026) and a high histological grade (p=0.026). COX-2 expression in both DCIS (n=25) and IBC (n=51) was significantly higher than in normal breast tissue (p<0.0001). In addition, the COX-2 expression rate was significantly higher in DCIS than in IBC (p=0.042). Our results indicated that COX-2 overexpression correlates with aggressive phenotypic features, such as HER-2/neu overexpression and high histological grade in IBC. Increased expression of COX-2 in both DCIS and IBC in comparison to normal breast could indicate a role in breast carcinogenesis. COX-2 overexpression may provide a clinically useful biomarker for estimating tumor aggressiveness.