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| **E.1 - The prognosis of GERD in infants and children** |
|  |  |  |  | Esophagitis at baseline | No esophagitis at baseline |
| *Microscopic* | *Macroscopic* | *Macroscopic* |  |
|  | **Outcome** | **In analysis** | **Follow-up time** | Orenstein et al. (n=19) | Shepherd et al.(n=126)# | El-Serag et al.(n=207) | Ruigomez et al.(n=1242) |
|  | Infants only(1.5-8.0 months) | Infants and children(2.5 months-10 years) | Children only(1-17 years) |
| **Clinical signs and symptoms** |
| - General | Persisting symptoms OR on GERD treatment at end of follow-up | 34/126 (27.0%)# | 18 months |  | 21/34(62%; p=NA) |  |  |
| 80/207 (38.6%) | > 5 years after initial diagnosis |  |  | 55/80(68.8%; p=NA) |  |
| 16/19 (84.2%) | 12 months  | 6/16(37.5%; p=NA) |  |  |  |
| - I-GERQ-R  | > 7 | 10/19\*(52.6%) | 12 months | 0/10(0%; p=0.001) |  |  |  |
| - Crying  | > 1 hour of the day | 1/10(10.0%; p=0.007) |  |  |  |
| - Regurgitation | > 3 times per day | 0/10(0%; p=0.01) |  |  |  |
| Monthly in past year | 80/207 (38.6%) | >5 years after initial diagnosis |  |  | 45/80(56.3%; p=NA) |  |
| Weekly in past year |  |  | 5/80(6.3%; p=NA) |  |
| - Heartburn | Monthly in past year |  |  | 64/80(80.0%; p=NA) |  |
| Weekly in past year |  |  | 16/80(20.0%; p=NA) |  |
| **Endoscopic complications**  |
| - Esophagitis | Macroscopic | 14/207 (6.8%) | >5 years after initial diagnosis |  |  | 3/14(21.4%;p=NA) |  |
| Microscopic | 10/19 (52.6%) | 12 months | 10/10(100%; p=NA) |  |  |  |
| Not specified | 1242/1242 (100%) | 4 ± 1.9 years |  |  |  | 18/1242(1.4%;p=NA) |
| - Barret’s esophagus | Intestinal metaplasia in columnar-lined esophagus  | 14/207 (6.8%) | >5 years after initial diagnosis |  |  | 0/14(0% p=NA) |  |
| Not specified | 1242/1242 (100%) | 4 ± 1.9 years |  |  |  | 0/1242(0%;p=NA) |
| NA=not available; I-GERQ-R = Infant Gastroesophageal Reflux Questionnaire Revised. #Data only provided for those patients with proven esophagitis (macroscopically) at baseline (n=34). \*Analysis included only those patients (n=10) that did not require rescue medication and were not withdrawn from the study during the 12 months of follow-up. |

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| **F.2 - What are prognostic factors in infants and children with GERD?** |
| **Prognostic factor** | **Outcome** | **Determinant** | **Results; n, %** | **p-value** |
| **Clinical signs and symptoms (El-Serag et al.)** |
| **Gender** | Weekly heartburn or regurgitation | MaleFemale | 6/32 (19%)12/48 (25%) | 0.51 |
| **Age of onset GERD** |  | ≤ 5 years> 5 years | 17/54 (31%)1/26 (4%) | **0.03** |
| **Ethnic group** |  | CaucasianNon-Caucasian | 13/58 (22%)4/22 (18%) | 0.98 |
| **Family history** |  | YesNo | 7/29 (24%)11/51 (22%) | 0.79 |
| **Endoscopic complications (Ruigomez et al.)** |
| **Gender** | Esophagitis (not specified) | MaleFemale | 52/632 (19%)47/629 (7.6%) | > 0.10 (\*p = 0.62) |
| **Age of onset GERD** |  | ≤ 5 years5 – 11 years12 – 17 years | 27/261 (10.3%)26/310 (8.4%)46/671 (6.9%) | > 0.10 (\*p = 0.20) |
| **Visits to PCP** |  | 1 – 34 – 10> 10 | 32/434 (7.4%)44/552 (8.0%)23/256 (9.0% | > 0.01 (\*p = 0.66) |
| **Initial diagnosis** |  | HeartburnGERD | 17/458 (3.7%)82/784 (10.5%) | **< 0.005**  |
| **Acid suppressants at time of diagnosis** |  | NoAntacids onlyH2RA +/- antacidsPPI +/- antacidsH2RA + PPI +/- antacids | 17/261 (6.5%)23/480 (4.8%)20/245 (8.2%)32/220 (14.5%)7/36 (21.2%) | **< 0.005** |

GERD = gastroesophageal reflux disease; PCP = primary care physician; H2RA = Histamine Receptor Antagonist; PPI = proton pump inhibitor

\*p: Indicates p-value calculated manually by using *Χ2 - test* based upon original data (no level of significance specified in original study).