Systematic Review and Meta-Analysis of the Sensitivity and Specificity of TTG and EMA IgA antibodies for persistent mucosal damage in persons with celiac disease following a gluten-free diet: Literature search documentation

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The following literature search report has been conducted using the STARLITE method. [1]

SAMPLING STRATEGY

- The systematic review hypothesis of concern is categorized as a diagnostic test question; as such, all relevant study designs including observational were included
- The primary investigator (JS) provided prior to the search investigation an established list of citations known to the investigator that met the inclusion criteria in the study proposal (*see List of References to Determine Search Validity*)
- Database selection was based on question type, and study designs of interest, consequently sampling expanded beyond clinical literature to include trial registry (clinical trials.gov) and basic biological sciences (BIOSIS)
- Conference proceedings were not desired by the primary investigator (JS) thus no gray literature and hand searching was conducted
- Date limits were established after initial sampling was conducted to confirm when specific tests came into use
- Possible strategies used by the Cochrane Upper Gland Pancreatic Diseases group was explored but none available
- Analysis of the results utilizing the validity set determined that the strategy include various combinations of the following concepts: disease, serology, diet, histology, follow-up – see also *Terms Used*

List of References to Determine Search Validity

1. Ciacci, C., Cirillo, M., Cavallaro, R., & Mazzacca, G. (2002). **Long-term follow-up of celiac adults on gluten-free diet: prevalence and correlates of intestinal damage**. *Digestion, 66*(3), 178-185. doi: 66757
2. Dewar, D. H., Donnelly, S. C., McLaughlin, S. D., Johnson, M. W., Ellis, H. J., & Ciclitira, P. J. (2012). **Celiac disease: management of persistent symptoms in patients on a gluten-free diet**. *World journal of gastroenterology : WJG, 18*(12), 1348-1356. doi: 10.3748/wjg.v18.i12.1348

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[1] Booth, A. 2006. "Brimful of STARLITE": towards standards for reporting literature searches. J Med Lib Assoc, October; 94(4): 421-429. Available at:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1629442/pdf/i1536-5050-094-04-0421.pdf

3. Hopper, A. D., Hadjivassiliou, M., Hurlstone, D. P., Lobo, A. J., McAlindon, M. E., Egner, W., . . . Sanders, D. S. (2008). **What is the role of serologic testing in celiac disease? A prospective, biopsy-confirmed study with economic analysis**. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association, 6*(3), 314-320. doi: 10.1016/j.cgh.2007.12.008

4. Kaukinen, K., Sulkanen, S., Maki, M., & Collin, P. (2002). **IgA-class transglutaminase antibodies in evaluating the efficacy of gluten-free diet in coeliac disease**. *European journal of gastroenterology & hepatology, 14*(3), 311-315.

5. Rubio-Tapia, A., Rahim, M. W., See, J. A., Lahr, B. D., Wu, T. T., & Murray, J. A. (2010). **Mucosal recovery and mortality in adults with celiac disease after treatment with a gluten-free diet**. *The American Journal of Gastroenterology, 105*(6), 1412-1420. doi: 10.1038/ajg.2010.10

6. Selby, W. S., Painter, D., Collins, A., Faulkner-Hogg, K. B., & Loblay, R. H. (1999). **Persistent mucosal abnormalities in coeliac disease are not related to the ingestion of trace amounts of gluten**. *Scandinavian journal of gastroenterology, 34*(9), 909-914.

7. Tonutti, E., Visentini, D., Picierno, A., Bizzaro, N., Villalta, D., Tozzoli, R., . . . Brusca, I. (2009). **Diagnostic efficacy of the ELISA test for the detection of deamidated anti-gliadin peptide antibodies in the diagnosis and monitoring of celiac disease**. *Journal of clinical laboratory analysis, 23*(3), 165-171. doi: 10.1002/jcla.20313

8. Tursi, A., Brandimarte, G., & Giorgetti, G. M. (2003). **Lack of usefulness of anti-transglutaminase antibodies in assessing histologic recovery after gluten-free diet in celiac disease**. *Journal of clinical gastroenterology, 37*(5), 387-391.

9. Vahedi, K., Mascart, F., Mary, J. Y., Laberenne, J. E., Bouhnik, Y., Morin, M. C., . . . Matuchansky, C. (2003). **Reliability of antitransglutaminase antibodies as predictors of gluten-free diet compliance in adult celiac disease**. *The American Journal of Gastroenterology, 98*(5), 1079-1087. doi: 10.1111/j.1572-0241.2003.07284.x

TYPES OF STUDIES

- No study design filter/limit was applied
- Primary research was only considered: see also *Inclusion and Exclusions*
- Investigative methods appropriate for laboratory methodology:
    - Randomized controlled trial
    - Case-control
    - Cohort
    - Cross-sectional

APPROACHES: Not applicable

RANGE OF YEARS

- Initial strategy did not include date limit; date ranges in databases include 1966- (PubMed), 1970- (Science Citation Index, Web of Science), 1971 – (Scopus), and 1974 – (Embase)
- Two updates:
    - January 2012 (initial search ended in mid 2012) to January 2016
    - January 2016 – January 2017

LIMITS
- English and Human

Szwajcer, Silvester – SR Sensitivity and Specificity of TTG and EMA IgA antibodies: Literature Search Documentation (2016)

INCLUSION AND EXCLUSIONS

Inclusion:
- Studies that describe diagnostic, prognostic, sensitivity and specificity qualities of serum-based celiac antibody tests
- Studies published in adult or pediatric populations
- Studies describing detection of mucosal damage via dietary assessment in patients prescribed or on gluten-free diet

Exclusion:
- Studies describing only celiac tests for diagnosis of celiac disease
- Involve animals
- Human-based studies that either do not have biopsy-proven diagnosis of celiac, or have not been prescribed a gluten-free diet
- Studies reporting use of an index standard other than the reference standard of small intestinal histopathology/biopsy and the measurement of celiac antibodies in tissues/samples other than blood
- Studies not reporting primary research; case or case-series reports

ELECTRONIC SOURCES: PubMed Medline; Embase (OVID); CENTRAL (Cochrane Library, Wiley); Science Citation Index (Web of Science, ISI); Scopus (Elsevier); BIOSIS Previews (Web of Science, ISI); ClinicalTrials.gov

TERMS USED/STRATEGIES:

PubMed

#1 ((celiac disease[MeSH Terms])) OR (coeliac disease[tiab] OR celiac disease[tiab])

#2 (((("Serologic Tests"[Mesh:noexp])) OR (((("Antibodies"[Mesh:noexp]) OR "Antibodies, Anti-Idiotypic"[Mesh]) OR ((("Immunoglobulins"[Mesh:noexp]) OR "Immunoglobulin A"[Mesh:noexp]) OR "Immunoglobulin G"[Mesh:noexp])) AND ("Transglutaminases"[Mesh:noexp]))) OR (((("Immunoglobulins"[Mesh:noexp]) OR "Immunoglobulin A"[Mesh:noexp]) OR "Immunoglobulin G"[Mesh:noexp]) AND (("Enzyme-Linked Immunosorbent Assay"[Mesh:noexp]) OR ("Fluorescent Antibody Technique"[Mesh:noexp])))) OR (((IgA antitransglutaminase[Title/Abstract]) OR (anti tissue transglutaminase[tiab] OR anti-tissue transglutaminase[tiab]) OR (tissue transglutaminase[tiab] OR tTG[tiab]) OR (IgA-class[tiab] AND transglutaminase[tiab]) OR (anti-tTG[tiab] OR anti tTG[tiab])) OR ((immunoglobulin G antibod*[tiab] OR IgG antibod*[tiab]) OR (immunoglobulin A antibod*[tiab] OR IgA antibod*[tiab])) OR ((anti gliadin antibod*[tiab] OR anti-gliadin antibod*[tiab]) OR (AGA[tiab] OR antigliadin[tiab]) OR (IgA-antigliadin antibody[tiab]) OR (((immunoglobulin G antibod*[tiab] OR IgG antibod*[tiab]) OR (immunoglobulin A antibod*[tiab] OR IgA antibod*[tiab])) AND ELISA[tiab])) OR ((antiendomysial antibod*[tiab] OR EMA[tiab]) OR (anti-endomysium[tiab] OR anti endomysium[tiab] OR antiendomysium[tiab]) OR (IgA-endomysial antibod*[tiab] OR IgA endomysial antibod*[tiab]) OR (IgA-EMA[tiab])) OR

((deamidated gliadin peptide antibody[tiab])) OR (a-DGP immunoglobulin A[tiab] OR a-DGP IgA[tiab]) OR (deamidated gliadin peptide*[tiab] OR DGP[tiab])) OR (serologic* AND test*[tiab] OR serologic* AND analysis[tiab] OR serologic* AND response[tiab]) OR ((serologic* AND test*[tiab] OR serologic* AND analysis[tiab] OR serologic* AND response[tiab]) AND ((immunoglobulin A[tiab] OR IgA[tiab]) OR (immunoglobulin G[tiab] OR IgG[tiab]))) OR (antibodies[tiab] AND (IgA-gliadin[tiab] OR IgG- gliadin[tiab])))

#3 (glutens[mh]) OR (diet, gluten-free[mh]) OR (gluten-free diet[tiab] OR gluten free diet[tiab]) OR (GFD[tiab])

#4 (((biopsy[mh]) AND ((duodenum[mh]) OR (intestinal mucosa[mh]))) OR ((biopsy[tiab]) AND (((small-bowel[tiab] OR small bowel[tiab])) OR (duoden*[tiab]) OR (intestinal[tiab]) OR ((small intestin*[tiab] OR small-intestin*[tiab]))))) OR ((small intestin*[tiab] OR small-intestin*[tiab]) AND morphology[tiab])

#5 ("follow up studies"[MeSH Terms]) OR (patient compliance[mh]) OR (time factors[mh]) OR (follow-up[tiab] OR follow up[tiab] OR followup[tiab]) OR (complian*[tw] OR comply[tw] OR complied[tw] OR non-complian*[tw] OR noncomplian*[tw]) OR ((complian*[tw] OR comply[tw] OR complied[tw] OR non-complian*[tw] OR noncomplian*[tw]) OR (adher*[tw] OR non-adher*[tw] OR nonadher*[tw])) OR (monitor*[tiab])

#6 #1 AND #3 AND #4
#7 #1 AND #2 AND #5
#8 #1 AND #3 AND #5
#9 #6 OR #7 OR #8

Embase

1   exp celiac disease/
2   c?eliac disease.ti,ab.
3   1 or 2
4   gluten/
5   gluten free diet/
7   GFD.ti,ab.
8   4 or 5 or 7
9   exp celiac disease/
10   c?eliac disease.ti,ab.
11   9 or 10
12   serodiagnosis/ or serology/
13   immunoglobulin antibody/ or immunoglobulin a antibody/ or immunoglobulin g antibody/
14   antibody/ or antiidiotypic antibody/
15   protein glutamine gamma glutamyltransferase antibody/
16   protein glutamine gamma glutamyltransferase/
17   15 or 16
18   enzyme linked immunosorbent assay/
19   fluorescent antibody technique/ or immunofluorescence test/
20   13 or 14
21   17 and 20
22   18 or 19
23   13 and 22
24   12 or 21 or 23

25   (IgA antitransglutaminase or IgA anti-transglutaminase or IgA anti transglutaminase).ti,ab. (68)

26   (anti tissue transglutaminase or anti-tissue transglutaminase).ti,ab. (671)

27   (tissue transglutaminase or tTG).ti,ab. (4147)

28   (IgA-class adj transglutaminase).ti,ab. (2)

29   (anti-tTG or anti tTG).ti,ab. (508)

30   25 or 26 or 27 or 28 or 29 (4189)

31   (anti gliadin antibod$ or anti-gliadin antibod$).ti,ab. (272)

32   (AGA or antigliadin or anti-gliadin or anti gliadin).ti,ab. (10379)

33   IgA-antigliadin antibody.ti,ab. (20)

34   (immunoglobulin A antibod$ or IgA antibod$).ti,ab. (3773)

35   (immunoglobulin G antibod$ or IgG antibod$).ti,ab. (17734)

36   34 or 35 (20635)

37   ELISA.ti,ab. (161568)

38   36 and 37 (5502)

39   31 or 32 or 33 or 38 (15822)

40   (antiendomysial antibod$ or EMA or anti-endomysial antibod$ or anti endomysial antibod$).ti,ab. (8252)

41   (IgA-endomysial antibod$ or IgA endomysial antibod$).ti,ab. (67)

42   IgA-EMA.ti,ab. (162)

43   endomysium antibody/ (1978)

44   40 or 41 or 42 or 43 (9465)

45   deamidated gliadin peptide antibody.ti,ab. (10)

46   (a-DGP immunoglobulin A or a-DGP IgA).ti,ab. (3)

47   (deamidated gliadin peptide$ or DGP).ti,ab. (544)

48   45 or 46 or 47 (544)

49   (serologic$ test$ or serologic$ analysis or serologic$ response).ti,ab. (14823)

50   (immunoglobulin A or IgA).ti,ab. (34627)

51   (immunoglobulin G or IgG).ti,ab. (96355)

52   50 or 51 (114453)

53   49 and 52 (2460)

54   ((IgA-gliadin adj2 antibod$) or (IgG-gliadin adj2 antibod$)).ti,ab. (28)

55   53 or 54 (2485)

56   24 or 30 or 39 or 44 or 48 or 55 (97285)

57   exp follow up/ (906998)

58   patient compliance/ (94632)

59   time/ (221939)

60   (follow-up or follow up or followup).ti,ab. (882873)

61   (complian$ or comply or complied or non-complian$ or noncomplian$).ti,ab. (131975)

62   (adher$ or non-adher$ or nonadher$).ti,ab. (150343)

63   61 or 62 (271854)

64   monitor$.ti,ab. (625081)

65   57 or 58 or 59 or 60 or 63 or 64 (2149033)

66   11 and 56 and 65 (1234)

67   8 and 11 and 65 (1952)

68   exp duodenum biopsy/ or exp intestine biopsy/ or biopsy/ (118862)

69   intestine mucosa/ (16194)

70   biopsy.ti,ab. (254942)

71   (small-bowel or small bowel).ti,ab. (28392)
72   duodenal.ti,ab. (32031)
73   intestinal.ti,ab. (173634)
74   (small intestin$ or small-intestin$).ti,ab. (39975)
75   71 or 72 or 73 or 74 (234582)
76   70 and 75 (11841)
77   68 or 69 or 76 (138445)
78   morphology.ti,ab. (19906)
79   74 and 78 (1101)
80   77 or 79 (139321)
81   3 and 8 and 80 (2731)
82   66 or 67 or 81 (4195)
83   limit 82 to yr="2012 -Current" (1584)
84   limit 83 to english language (1523)
85   limit 84 to (embase and article) (524)
86   from 84 keep 1-1523 (1523)

CENTRAL

#1   MeSH descriptor: [Celiac Disease] explode all trees
#2   "coeliac disease" or "celiac disease":ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Antibodies] this term only
#5   MeSH descriptor: [Antibodies, Anti-Idiotypic] this term only
#6   #4 or #5
#7   MeSH descriptor: [Immunoglobulin G] this term only
#8   MeSH descriptor: [Immunoglobulins] this term only
#9   MeSH descriptor: [Immunoglobulin A] this term only
#10   #7 or #8 or #9
#11   MeSH descriptor: [Transglutaminases] this term only
#12   MeSH descriptor: [Enzyme-Linked Immunosorbent Assay] this term only
#13   MeSH descriptor: [Fluorescent Antibody Technique] this term only
#14   MeSH descriptor: [Serologic Tests] this term only
#15   (#6 or #10) and #11
#16   (#12 or #13) and #10
#17   #14 or #15 or #16
#18   "anti-tissue transglutaminase":ti,ab,kw (Word variations have been searched)
#19   "tissue transglutaminase" or tTG:ti,ab,kw (Word variations have been searched)
#20   IgA-class transglutaminase:ti,ab,kw (Word variations have been searched)
#21   anti-tTG:ti,ab,kw (Word variations have been searched)
#22   #18 or #19 or #20 or #21
#23   anti-gliadin antibod*:ti,ab,kw (Word variations have been searched)
#24   AGA or antigliadin:ti,ab,kw (Word variations have been searched)
#25   IgA-antigliadin antibody:ti,ab,kw (Word variations have been searched)
#26   immunoglobulin A antibod* or IgA antibod*:ti,ab,kw (Word variations have been searched)
#27   immunoglobulin G antibod* or IgG antibod*:ti,ab,kw (Word variations have been searched)

#28   ELISA or enzyme-linked immunosorbent assay:ti,ab,kw (Word variations have been searched)

#29   (#26 or #27) and #28

#30   #23 or #24 or #25 or #28

#31   antiendomysial antibod* or EMA or anti-endomysium:ti,ab,kw (Word variations have been searched)

#32   deamidated gliadin peptide antibody or a-DGP immunoglobulin A or a-DGP IgA or deamidated gliadin peptide* or DGP:ti,ab,kw (Word variations have been searched)

#33   serologic* test* or serologic* analysisOR serologic* response:ti,ab,kw (Word variations have been searched)

#34   (#26 or #27) and #33

#35   antibodies and (IgA-gliadin or IgG-gliadin):ti,ab,kw (Word variations have been searched)

#36   #17 or #22 or #30 or #31 or #32 or #34 or #35

#37   MeSH descriptor: [Glutens] explode all trees

#38   MeSH descriptor: [Diet, Gluten-Free] explode all trees

#39   gluten-free diet or GFD:ti,ab,kw (Word variations have been searched)

#40   #37 or #38 or #39

Science Citation Index (Web of Science)

#1   (TS=("coeliac disease" OR "celiac disease")) AND Language=(English) AND Document Types=(Article)

#2   (TS=(antibod*)) AND Language=(English) AND Document Types=(Article)

#3   (TS=(Immunoglobulin? OR "Immunoglobulin A" OR "Immunoglobulin G" OR IgA OR IgG)) AND Language=(English) AND Document Types=(Article)

#4   (TS=(transglutaminase?)) AND Language=(English) AND Document Types=(Article)

#5   (TS=("Enzyme-Linked Immunosorbent Assay" OR "enzyme linked immunosorbent assay" OR ELISA)) AND Language=(English) AND Document Types=(Article)

#6   (TS=("Fluorescent Antibody" NEAR/1 Technique) OR TS=("Fluorescent Antibody" NEAR/1 Test)) AND Language=(English) AND Document Types=(Article)

#7   ((#2 OR #3) AND #4) AND Language=(English) AND Document Types=(Article)

#8   ((#5 OR #6) AND #3) AND Language=(English) AND Document Types=(Article)

#9   #8 OR #7

#10   (TS=(IgA NEAR/1 antitransglutaminase) OR TS=("anti tissue" NEAR/1 transglutaminase) OR TS=(anti-tissue NEAR/1 transglutaminase) OR TS=("tissue transglutaminase" OR tTG) OR TS=(IgA-class NEAR/1 transglutaminase) OR TS=(anti-tTG OR "anti tTG")) AND Language=(English) AND Document Types=(Article)

#11   (TS=("immunoglobulin A" NEAR/1 antibod*) OR TS=(IgA NEAR/1 antibod*) OR TS=("immunoglobulin G" NEAR/1 antibod*) OR TS=(IgG NEAR/1 antibod*)) AND Language=(English) AND Document Types=(Article)

#12   (TS=("anti gliadin" NEAR/1 antibod*) OR TS=(anti-gliadin NEAR/1 antibod*) OR TS=(AGA OR antigliadin)) AND Language=(English) AND Document Types=(Article)

#13   #11 AND #5

#14   #13 OR #12

#15   (TS=(antiendomysial NEAR/1 antibod*) OR TS=(EMA) OR TS=(anti-endomysium OR "anti endomysium" OR antiendomysium) OR TS=(IgA-EMA)) AND Language=(English) AND Document Types=(Article)

#16   (TS=("deamidated gliadin peptide antibody") OR TS=("deamidated gliadin" NEAR/1 peptide*) OR TS=DGP OR TS=("immunoglobulin A" NEAR/1 a-DGP) OR TS=(IgA NEAR/1 a-DGP)) AND Language=(English) AND Document Types=(Article)

#17   (TS=(serologic*NEAR/1 test) OR TS=(serologic* NEAR/1 analysis) OR TS=(serologic* NEAR/1 response) OR TS=(serum NEAR/1 test) OR TS=(serum NEAR/1 analysis)) AND Language=(English) AND Document Types=(Article)

#18   #17 AND #3

#19   #18 OR #16 OR #15 OR #14 OR #10 OR #9

#20   (TS=(gluten) OR TS=(glutens) OR TS=(gluten-free NEAR/1 diet) OR TS=("gluten free" NEAR/1 diet) OR TS=GFD) AND Language=(English) AND Document Types=(Article)

#21   (TS=biopsy) AND Language=(English) AND Document Types=(Article)

#22   (TS=duodenum OR TS=("intestinal mucosa") OR TS=(small-bowel OR "small bowel") OR TS=intestin*) AND Language=(English) AND Document Types=(Article)

#23   (TS=(small NEAR/1 intestin*) OR TS=small-intestin*) AND Language=(English) AND Document Types=(Article)

#24   #23 OR #22

#25   #24 AND #21

#26   (TS=morphology) AND Language=(English) AND Document Types=(Article)

#27   #26 AND #23

#28   #27 OR #25

#29   (TS=("patient compliance") OR TS=(follow-up OR "follow up" OR followup) OR TS=(complian* OR comply OR complied OR non-complian* OR noncomplian*) OR TS=(adher* OR non-adher* OR nonadher*) OR TS=monitor*) AND Language=(English) AND Document Types=(Article)

#30   #29 AND #20 AND #1

#31   #29 AND #19 AND #1

#32   #28 AND #20 AND #1

#33   #32 OR #31 OR #30