

Global perspective of coeliac disease with a focus on Asia

Coeliac disease: Past, Present, Future; 50th years celebration Coeliac UK

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Coeliac disease: Then

- Initially thought to be limited to the Western Europe
- Seen only/mainly by pediatricians
- Making a diagnosis was TEDIOUS

While the curative treatment was known, but making the diagnosis was a challenge



1980 - 2000

- Change in the diagnostic criteria: three biopsies to one biopsy
- Advent of serology
- Wider recognition: Pediatrician to Adults

Recognised in countries having Caucasian population



Coeliac disease: Now

Changing epidemiology globally

Clinical Gastroenterology and Hepatology 2017; =: =-

Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis

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Global prevalence: systematic review and meta-analysis

Included studies in whom at least 50% of seropositive individuals were biopsied for calculation of prevalence of CD



Singh P, Clin Gastroenterol Hepatol, In press

Global seroprevalence of CeD



Study	Events	Total	Events per 100 observations	Events	95%-CI	Weig
Aljebreen 2013	26	1167		2.23	[1.46; 3.25]	1.0
Khayyat 2012	3	204		1.47	[0.30; 4.24]	0.8
Akbari 2006	29	2799		1.04	[0.69; 1.48]	1.1
Bdioui 2006	3	1418		0.88	[0.46; 1.46]	
Dalgic 2011	489	20190		2.42	[2.21; 2.64]	1.1
Dehghani 2013	30	1500		2.00	[1.35; 2.84]	1.1
Gursoy 2005	48	906		5.30	[3.93; 6.96]	1.0
Ertekin 2006 Rep Hariz 2007	11	1263	and a second sec	0.87	[0.44; 1.55]	1.0
Israeli 2010	139	850		1.06	[0.49: 2.00]	1.0
Kochhar 2012	9	1610	ter l	0.56	[0.26; 1.06]	1.1
Makharia 2011	50	2879		1.74	[1.29; 2.28]	1.1
Nusier 2010	30	1985		1.51	[1.02; 2.15]	1.1
Yan 2015	16	562		2.85	[1.64: 4.58]	1.0
Shamir 2002	56	1571		3.56	[2.70; 4.60]	1.1
Saberi-Firouzi 2008	7	1440		0.49	[0.20; 1.00]	1.1
Demirçeken 2008	10	1000		1.00	[0.48; 1.83]	1.0
Alarida 2011	3	2020	and a second sec	0.47	[0.10; 1.38]	1.1
Alencar 2012	24	4000		0.60	[0.38; 0.89]	1.1
Almeida 2012	0	840		0.00	[0.00; 0.44]	1.0
Almeida 2013	10	946		1.06	[0.51; 1.94]	1.0
Antunes 2002	11	536	and a second sec	2.05	[1.03; 3.64]	1.0
Bonamico 2011	40	4048		2.50	[0 71: 1 34]	
Carlsson 2001	13	690		1.88	[1.01; 3.20]	1.0
Carlsson 2006	19	679		2.80	[1.69; 4.34]	1.0
Castaño 2004	10	484		2.07	[1.00; 3.77]	1.0
Catassi 1999	56	989		5.66	[4.31; 7.29]	1.0
Chin 2009	47	3011		1.56	[1 15: 2 07]	
Cook 2000	12	1064		1.13	[0.58; 1.96]	1.0
Crovella 2007	25	1074		2.33	[1.51; 3.42]	1.0
Csizmadia 1999	75	6127		1.22	[0.96; 1.53]	1.1
Edlinger-Horvat 2005	76	7660		0.98	[0.77; 1.23]	1.1
Eabiani 2004	102	3541		2.88	[2 35: 3 49]	1.1
Fasano 2003	31	4126		0.75	[0.51; 1.06]	1.1
Galván 2009	1	200		0.50	[0.01; 2.75]	0.8
Johannsson 2009	6	813		0.74	[0.27; 1.60]	1.0
Hariz 2013	7	2064		0.34	[0.14; 0.70]	1.1
Koroonay_Szabó 1999	24	427		1.60	[1.03; 2.37]	0.9
Ivarsson 2013	291	12632	100	2.30	[2.05; 2.58]	1.1
Ivarsson 1999	9	1894		0.48	[0.22; 0.90]	1.1
Johnston 1998	22	1823		1.21	[0.76; 1.82]	1.1
Karagiozoglou-Lampoudi 2013	8	1080		0.74	[0.32; 1.45]	1.4
Kratzer 2013	14	2157		0.65	[0.36: 1.09]	1.1
Lagerqvist 2001	60	1850		3.24	[2.48; 4.16]	1.1
Mäki 2003	56	3654	100	1.53	[1.16; 1.99]	1.1
Mariné 2010	21	4230		0.50	[0.31; 0.76]	1.1
Mora 2012	29	2219	Ŧ	1.40	[0.88: 1.87]	1.1
Myléus 2009	192	7567	1 100	2.54	[2.19; 2.92]	1.1
Oliveria 2007	45	3000		1.50	[1.10; 2.00]	1.1
Pereira 2006	6	2086		0.29	[0.11; 0.62]	1.1
Pratesi 2003	16	4405	and the second s	0.36	[0.21; 0.59]	
Bess 2007	5	1160	-	0.43	[0.14: 1.00]	1.0
García Novo 2007	11	2215		0.50	[0.25; 0.89]	1.1
Cilleruelo Pascual 2002	15	3378	Mi	0.44	[0.25; 0.73]	1.1
Remes-Troche 2006	27	1009		2.68	[1.77; 3.87]	1.0
Boka 2007	20	2230	-	0.17	[0.02; 0.62]	1.1
Rostami 1999	3	1000		0.30	[0.06; 0.87]	1.0
Rutz 2002	11	1450	100	0.76	[0.38; 1.35]	1.1
Stroikova 2006	41	1740		2.36	[1.70; 3.18]	1.1
Szanarska-Pop. awska 2009 Bubio Tania 2012	25	3235		0.63	[0.50; 1.14]	
Tikkakoski 2007	33	1900		1.74	[1.20; 2.43]	1.1
Tommasini 2004	48	3188	-	1.51	[1.11; 1.99]	1.1
Trevisiol 2004	121	1030		- 11.75	[9.84; 13.87]	1.0
Volta 2001	20	3483		0.57	[0.35; 0.89]	1.1
Vanciková 2002	112	1312		8.54	17.08:10.18	1.0
Mustalahti 2010	123	6403		1.92	[1.60; 2.29]	1.1
Mustalahti 2010	18	4173	122 ····	0.43	[0.26; 0.68]	1.1
Mustalahti 2010	98	7126		1.38	[1.12; 1.67]	1.1
Mustalahti 2010	18	1975		0.91	[0.54; 1.44]	
Corazza 1997	4	2237		0.18	[0.51; 1.63]	1.1
Korponay-Szabó 2007	42	2690		1.56	[1.13; 2.10]	1.1
Kondrashova 2008	12	1988	111 ·	0.60	[0.31; 1.05]	1.1
Cataldo 2002	0	600	- Law	0.00	[0.00; 0.61]	1.0
Gaivan 2010	7	595		1.18	[0.47; 2.41]	1.0
Al Hatlani 2015	32	1141		2.80	[1.93: 3.94]	10
Ramakrishna 2016	1709	23331		7.33	[6.99; 7.67]	1.1
Almazán 2015	6	198		3.03	[1.12; 6.48]	0.8
Gesualdo 2016	7	200		3.50	[1.42; 7.08]	9.0
Laass 2015	4	12741	13	2.78	0.76; 6.96	0.5
Lohi 2007	129	6402		2.01	[1.68; 2.39]	1.1
		0.02		2.51	[1000
Random effects model Heterogeneity: J ² = 98%, τ ² = 0.00	35. ρ < 0.	275818 D1	· • • • • • • • • • • • • • • • • • • •	1.37	[1.10; 1.68]	100.0

96 studies:275,818 subjects 5,571 positive for TG2/EMA

1.37% (95%CI 1.1%, 1.68%) 0% to 11.7%

Heterogeneity: 98%

Singh P, Clin Gastroenterol Hepatol, In press

Global prevalence of CeD

Study	Events	Total		Prop (in %)	95%-CI	W(random)
Corazza 1997	4	2237	*	0.18	[0.05; 0.46]	1.8%
Kolho 1998	8	1070	- 10	0.75	[0.32; 1.47]	1.7%
lvarsson 1999	10	1894		0.53	[0.25; 0.97]	1.8%
Csizmadia 1999	31	6127		0.51	[0.34; 0.72]	1.9%
Rostami 1999	3	1000		0.30	[0.06; 0.87]	1.7%
Korponay-Szabó 1999	5	427		1.17	[0.38; 2.71]	1.4%
Catassi 2000	18	2096		0.86	[0.51; 1.35]	1.8%
Riestra 2000	3	1170	100 C	0.26	[0.05; 0.75]	1.7%
Cook 2000	13	1064		1.22	[0.65; 2.08]	1.7%
Volta 2001	17	3483	1997 - C.	0.49	[0.28; 0.78]	1.9%
Carlsson 2001	8	690		1.16	[0.50; 2.27]	1.6%
Shamir 2002	10	1571		0.64	[0.31; 1.17]	1.8%
Rutz 2002	8	1450		0.55	[0.24; 1.08]	1.8%
Cilleruelo Pascual 2002	21	3378	the second secon	0.62	[0.39; 0.95]	1.9%
Mäki 2003	37	3654		1.01	[0.71; 1.39]	1.9%
Pratesi 2003	15	4405	+	0.34	[0.19; 0.56]	1.9%
El-Hadi 2004	6	1000	- 12	0.60	[0.22; 1.30]	1.7%
Castaño 2004	7	484	÷	1.45	[0.58; 2.96]	1.4%
Tommasini 2004	32	3188		1.00	[0.69; 1.41]	1.9%
Fabiani 2004	20	3541		0.56	[0.35; 0.87]	1.9%
Gursoy 2005	12	906		1.32	[0.69; 2.30]	1.6%
Bdioui 2006	2	1418	*	0.14	[0.02; 0.51]	1.8%
Akbari 2006	9	2799	+	0.32	[0.15; 0.61]	1.9%
Ertekin 2006	7	1263		0.55	[0.22; 1.14]	1.7%
Pereira 2006	5	2086	+	0.24	[0.08; 0.56]	1.8%
Menardo 2006	10	1002		1.00	[0.48; 1.83]	1.7%
Novo 2007	6	2215	+	0.27	[0.10; 0.59]	1.8%
Korponay-Szabó 2007	37	2690		1.38	[0.97; 1.89]	1.9%
Ress 2007	4	1160	-+	0.34	[0.09; 0.88]	1.7%
Vilppula 2008	60	2815		2.13	[1.63; 2.74]	1.9%
Demirçeken 2008	9	1000		0.90	[0.41; 1.70]	1.7%
Saberi-Firouzi 2008	2	1440	+	0.14	[0.02; 0.50]	1.8%
Kondrashova 2008	4	1988	2000 - Contra Co	0.20	[0.05; 0.51]	1.8%
Abu–Zekry 2008	15	1500		1.00	[0.56; 1.64]	1.8%
Galván 2009	1	200		0.50	[0.01; 2.75]	1.0%
Johannsson 2009	6	813		0.74	[0.27; 1.60]	1.6%
Chin 2009	14	3011		0.46	[0.25; 0.78]	1.9%
Myléus 2009	195	7567		2.58	[2.23; 2.96]	2.0%
Mariné 2010	21	4230	H	0.50	[0.31; 0.76]	1.9%
Bahari 2010	7	1600		0.44	[0.18; 0.90]	1.8%
Israeli 2010	6	850		0.71	[0.26; 1.53]	1.6%
Mustalahti 2010	43	7126		0.60	[0.44; 0.81]	2.0%
Mustalahti 2010	85	6403		1.33	[1.06; 1.64]	1.9%
Alarida 2011	20	2920	*	0.68	[0.42; 1.06]	1.9%
Bonamico 2011	46	4048		1.14	[0.83; 1.51]	1.9%
Makharia 2011	31	2879		1.08	[0.73; 1.52]	1.9%
Kochhar 2012	9	1610		0.56	[0.26; 1.06]	1.8%
Alencar 2012	14	4000		0.35	[0.19; 0.59]	1.9%
Mora 2012	28	2219		1.26	[0.84; 1.82]	1.8%
Farahmand 2012	3	634		0.47	[0.10; 1.38]	1.5%
Almeida 2012	0	840		0.00	[0.00; 0.44]	1.6%
Hariz 2013	5	2064	-	0.24	[0.08; 0.56]	1.8%
lvarsson 2013	329	12632		2.60	[2.33; 2.90]	2.0%
Karagiozoglou-Lampoudi 2013	7	1080		0.65	[0.26; 1.33]	1.7%
Kratzer 2013	8	2157	*	0.37	[0.16; 0.73]	1.8%
Dehghani 2013	9	1500	1	0.60	[0.27; 1.14]	1.8%
Almazán 2015	6	198		3.03	[1.12; 6.48]	1.0%
Random effects model		138792	<u> </u>	0.68	[0.52; 0.86]	100%
Heterogeneity: I^2=92.3%, tau^2=0.	005, p<0.0	001				

57 studies, 138, 792 patients

0.68%, 95% CI: 0.52-0.86

Singh P, Clin Gastroenterol Hepatol, In press





Differences between pooled global seroprevalence and prevalence of biopsyconfirmed CeD?

> Sero-prevalence: 1.37% Prevalence of CeD: 0.68%

Biopsy rate ranged from 51.2 to 100%

Under-estimation of actual CeD prevalence

Potential coeliac False positive Estimated number of patients with CeD globally



- Pooled prevalence of biopsy confirmed CeD: 0.68% (95% CI 0.5%, 0.9%)
- Global population 7.4 billion,
 - 37 million to 59 million individuals are likely to have CeD around the world
 - Globally, majority of patients (83%-95%)
 - Still remain undiagnosed

Singh P, Clin Gastroenterol Hepatol, In press



Prevalence: Continent wise

Continent wise prevalence



Location	No screened for sero- prevalence	sero +	Pooled sero- prevalence (95% CI)	No screened for biopsy proven CeD	Bx proven CeD	Pooled prevalence of CeD
Continents						
Europe	163,700	2340	1.3 (1.1, 1.5)	98, 391	1119	0.8 (0.6, 1.1)
N America	17,778	200	1.4 (0.7, 2.2)	200	01	0.5
S America	20,245	280	1.3 (0.5, 2.5)	16,550	69	0.3 (0.1, 0.6)
Asia	68,632	2607	1.8 (1, 2.9)	18,052	114	0.6 (0.4, 0.8)
Africa	15,775	253	1.1 (0.4, 2.2)	7902	42	0.8 (0.2, 1.7)
Oceania	4,075	59	1.4 (1.1, 1.8)	4075	27	0.5 (0.2, 0.9)

Singh P, Clin Gastroenterol Hepatol, In press

Prevalence: continent wise





Singh P, Clin Gastroenterol Hepatol, In press

CeD in world's top ten most populous countries



- Population based prevalence available only from four top ten populous countries
 - -India
 - -USA
 - -Brazil
 - -Russia

Lack of data from

- China
- Indonesia
- Pakistan
- Nigeria
- **Bangladesh**
- Japan

Sero-prevalence: country wise



Highest Q Algeria Czech Rep India Israel Saudi-Arabia Sweden Portugal Turkey



Lowest Q Estonia Germany Iceland Libya Poland Spain Switzerland

Singh P, Clin Gastroenterol Hepatol, In press

Prevalence of CeD: country-wise



Highest Q Argentina Egypt Hungary Finland India NZ Sweden



Singh P, Clin Gastroenterol Hepatol, In press



Children Vs Adults Difference in prevalence of biopsy confirmed CeD

- Of 57 studies, 43 reported separate pooled prevalence for pediatric pts and adult pts
- Pooled prevalence of CeD: (P<0.001)
 - -276 of 40,076 adults: 0.5% (95% CI 0.3, 0.8)
 - -891 of 65,957 children: 0.9% (95%CI 0.6, 1.3)

Summary: 1



- CeD is a global disease
- 1.37% of global population is seropositive
- 0.68% of the global population have biopsy confirmed CeD

- Underestimation of the disease
- Exclusion of studies in whom <50% were biopsied

Trend of prevalence of CeD



Two contexts

Has the prevalence of CeD plateaued, or still evolving

Emergence of CeD in new regions

Increasing prevalence over time



- Stratified the studies into 2 time periods:
 - January 1991 to December 2000
 - Jan 2001 onward (based on actual study period)
 - Studies overlapping 2 time periods: Deleted
 - 1991 to 2000: 0.6% (95% Cl, 0.5%–0.7%)
 - 2011 to March 2016: 0.8% (95% Cl, 0.5% 1%)

Singh P, Clin Gastroenterol Hepatol, In press

Prevalence almost doubled in Finland



Mini-Finland survey in 1978-80 Health 2000 survey in 2000-01 Eligible finnish -- Type 1 diabetes (y-axis on the left) 2 456 714 3 262 918 population - Coeliac disease (y-axis on the right) 0.35 2.5 Adult-representative 8000 8028 sample 0.30 -2.0 -1.5 Prevalence of coeliac disease (%) 2 0.25 Participants of the 7217 (90%) 6770 (84%) primary study (%) Levalence of type 1 0.10 Participants of this 6993 (87%) 6402 (80%) study with available serum sample (%) Tissue trans-123 577 glutaminase anti-0.05 body positives 0.00 0.0 Earlier Earlier Endomysial anti-1950 1960 1970 1980 2000 1990 2 74 92 32 diagnosed diagnosed body positive cases cases All coeliac disease 76 124 cases

Lohi S, Aliment Pharmacol Ther 2007;26: 1217–25



CeD is increasing in USA



Catassi C et al, Ann Med 2010



Rise in CeD: Why?

- Increase in awareness
- Advancement in the diagnostic tools
- Use of wheat in rice eating regions
- Increase in gluten content of infant feeding
 - Sweden epidemic (1985 to 1995)

Ivarsson A, Acta Paediatr2000;89: 165–



Summary: 2

In many countries, the prevalence has increased 2 to 4 fold over 20 - 30 yrs

Europe





Prevalence of CeD in children and adolescents in Germany.



- German Health Interview and Examination Survey for Children and Adolescents 2003-2006
- 12, 741 participants aged 1 to 17 years (6546 boys)
 - 9 (0.07%) had a reported history of CeD.
 - 98 anti-tTG positive on screening
- Prevalence of undiagnosed CeD (based on + serology): 0.8% (95% CI 0.6-1.0%),

Overall prevalence of the disease: 0.9%.

Laass MW, Detach Arztebl Int. 2015;112:553-60

Russia: still unexplored





Sparse reports on prevalence

Possibility of large burden of CeD in Russia, needs to be explored

CeD in Russia



Region	Year	Participants	Test	screened	CD
Karelia region	1997– 2001	School children	Anti-tTG	1988	1 : 496 (0.20%)
Ryazan region	ND	blood donors	Anti-tTG	1740	1 : 174 (0.57%)
Irkutsk region	2011	Specific risk [*]	Anti-tTG	1441	1 : 18 (5.56%)
		· · · · · · · *		1402	1:31 (3.32%)
	2014	Specific risk		1775	1 : 40 (2.50%)
Krasnodar region	2010	Specific risk [*]	Anti-tTG and/or AEA	742	1 : 36.6 (2.73%)
Moscow	2003–07	Specific risk [*]	Anti-tTG	363	1 : 6.2 (15.98%)
	2012	Specific risk ^{**}		318	1 : 106 (0.94%)
Nizhny Novgorod	2008	Specific risk [*]	Anti-tTG	1045	1 : 7.6 (13.16%)
Ryazan region	2002– 2006	Specific risk ^{***}	Anti-tTG	256	1 : 57 (1.75%)
		Lvudmila	V. Savvate	eva. J Immi	inol Res. 2017



CeD in Sub-Sahara





16 with positive AEA: All coeliac 56/989 AEA+: 5.6%

5 fold higher High gluten consumption High HLA-DQ2/DQ8

> Catassi, Lancet, 1999 Catassi, Tissue antigen, 2001



Asia



Map of CeD in Asian region



Cummins AG, J Gastroenterol Hepatol. 2009



India

India: Population-based study



Two stage screening: Symptoms-based questionnaire and serology Seropositive: Biopsy

Subgroup	Corrected seroprevalence (95% CI)	Corrected prevalence of CeD (95% CI)
Adults (<i>n = 6845</i>)	1.10% (0.86, 1.37)	0.85% (0.64, 1.09)
Children (<i>n= 3643</i>)	2.06% (1.62, 2.57)	1.41% (1.04, 1.84)
Males (n = 5305)	1.28% (1.00, 1.62)	0.91% (0.67, 1.20)
Females (<i>n</i> = 5183)	1.60% (1.28, 1.98)	1.20% (0.92, 1.53)

1.04% (One in 96)

Population prevalence of CeD in India



Investigators	Study	Νο	Prevalence
Sood et al, 2006	Population based study in children (Punjab)	4347	1 in 310 (O.3%)
Makharia, 2010	Population based study in adults (NCR)	2879	1 in 96 (1.04%)
Kochhar, 2015	Healthy blood donor	1610	1 in 179 (0.56%)
Singh P, JGH, 2016	Metaanalysis		0.6%

Regional differences



- Mostly in Northern part
- Few from Southern and North Eastern part of India.

- Is it dietary factor ?
- Genetic predisposition?



Indian population: 1.2 Billion







Inadequate biopsy: 7

Ramakrishna, AJG 2015



South Indians in USA: lowest prevalence Punjabis in USA: highest prevalence



National pathology laboratory 2008 and 2015. Prevalence of villous atrophy Algorithmic determination of ethnicity based on names

- Among all patients (n=454,885)
 - Overall prevalence: 1.74%.
 - Other Americans (n=380,163): 1.83%
- Lower prevalence in
 - Patients of South Indian (n=177, 0%; P=.08),
 - East Asian (n=4700, 0.15%; P=<.0001),
 - Hispanic (n=31,491, 1.06%; P=<.0001).
- Higher in pts from Punjab (n=617, 3.08%)
 - others North India (n=1195, 1.51%; P=.02).

Krugel A, Clin Gastroenterol and Hepatol, 2016



Why?

CeD in China: Unexplored



Traditional belief: No CeD in China

Study	Province	Patients	Criteria for diagnosis	No.	Prevalence
Wu J 2010, Rev Esp Enferm Dig.	Nanjing	IBS_D (72) IDDM (6)	lgA-AGA lgA-TTG	6/78 (AGA+) 2/78 (tTG+)	7.7% 2.6%
Wang XQ, 2010 Zhonghua Er Ke Za Zhi.	Shanghai	Chronic diarrhea	Clinical sypmtoms Duodenal Bx	14/118 suspected	12%
Xin-Qiong W, JPGN, 2011	Shanghai, Wuhan, Jinan, Chengdu	Children with Chr diarrhea		14/118	

19,778 undiagnosed Chinese adolescents and young adults (age, 16-25 y): 2.19% coeliac disease Ab positive Clin Gastroenterol Hepatol, 2017



CeD in IBS-D patients

- 246 IBS patients (North China) and 246 healthy controls.
- Screened with anti-tTG: Positive test: probe-based confocal laser endomicroscopy (pCLE) and duod Bx
- Sero-prevalence: 12 IBS (4.8%) & 2 controls (0.81%)
- 5 underwent pCLE and targeted biopsy; all CeD
- With GFD: Seven serologically positive clinical improvement,
- Minimum Prevalence of CeD: 2.85%.

Kou G, J Dig Dis. 2018 Feb 16

CeD in Japan



Yr	Diagnosis	n	Gluten Challenge Test or GFD	Serological Test	Biopsy Confirmed	HLA
1983	Celiac sprue, Gluten induced enteropathy	1	Yes(Gluten challenge, GFD)	No	Yes(villous atrophy)	No
1991	Celiac sprue	4	Yes (Gluten Challenge	No	Yes(villous atrophy)	No
1988 1993	Celiac disease	2	Yes (GFD)	No	Yes(villous atrophy)	No
2000	Celiac sprue	1	Yes (GFD)	No		No
2003	Celiac disease	1	No	No	No	No
2006	B-cell Lymphoma associated with celiac disease	1	Νο	positive for tTG	Yes(villous atrophy)	Yes (nonDQ2/8)
2007	T-cell Lymphoma associated with celiac disease	1	Νο	No	Yes(villous atrophy)	No

Courtsey, Watanabe C

Sero-prevalence of CeD in IBD: Japan





IBD: anti-tTG Ab and anti-DGP Ab: 22 (12.8%) and 23 (13.4%) Controls (n=172): 3 (1.6%) and 1(0.5%),



CeD in Malaysia



- 562 Healthy young volunteers (mean age 24 \pm 2.4 yrs)
- Screening for CeD: Two stages
 - First step: IgG/IgA AGA and anti-tTG IgA/IgG.
 - Second step: Testing of positive samples by EmA.
- Definition of CeD: Both positive
- Seroprevalence of CeD: 1.25% (95% CI, 0.78-1.72) (7 of 562)
 - Median AGA: 38.2 U/ml (IQR, 28.3–60.4 U/ml)
 - IgA anti-tTG Ab: 49.2 U/ml (IQR, 41.1–65.9 U/ml)

Malay: 0.8% (2 of 236), Chinese: 1.7% (3 of 177) Indian: 1.3% (2 of 149)

Sero-prevalence of CeD: 1.25% (1 in 100) CD is underdiagnosed, Could be a much greater problem Population based studies: Eastern/Southern Asia



Sood A, Healthy school children (n=4347): 0.32% Makharia; 2011, General population (n=10488): 1.04% Ramakrishna, 2015 (n>23000): 0.67% Kochhar,2012, Healthy blood donors : 0.56%



Population based studies: Middle East/West Asia





Asian countries: Case report/case series





No reports from







Pooled seroprevalence of CeD in Asia: Systematic review

Study ID		Percent (95% CI)	% Weight
Shamir (2002)		3.56 (2.70, 4.60)	5.12
Tatar (2004)		1.30 (0.85, 1.90)	6.06
Gursoy (2005)	_ -	5.30 (3.93, 6.96)	3.82
Ertekin (2006)	+	0.87 (0.44, 1.55)	5.99
Sood (2006)	•	0.48 (0.30, 0.74)	6.48
Akbari (2006)	+	1.04 (0.69, 1.48)	6.27
Saberi-Firouzi (2008)	←	0.49 (0.20, 1.00)	6.26
Demerciken (2008)		1.00 (0.48, 1.83)	5.75
Israeli (2010)	-+ <u>+</u> -	1.06 (0.49, 2.00)	5.57
Bahari (2010)	-	0.88 (0.48, 1.46)	6.11
Nusier (2010)		1.51 (1.02, 2.15)	5.98
Makharia (2011)	+	1.74 (1.29, 2.28)	6.11
Dalgic (2011)	•	2.42 (2.21, 2.64)	6.49
Khayyat (2012)		1.47 (0.30, 4.24)	2.96
Kochhar (2012)	←	0.56 (0.26, 1.06)	6.26
Aljebreen (2013)		2.23 (1.46, 3.25)	5.26
Dehghani (2013)	+ •−	2.00 (1.35, 2.84)	5.60
Yap (2015)		2.85 (1.64, 4.58)	3.91
Overall (I-squared = 93.4%, p = 0.000)	•	1.58 (1.13, 2.04)	100.00
NOTE: Weights are from random effect	s analysis		
C)12345		

Prashant Singh, et al, JGH 2016



Pooled prevalence of CeD in Asia: Systematic review

Study			%
ID		Percent (95% CI)	weight
Shamir (2002)		0.64 (0.31, 1.17)	5.51
Tatar (2004)	•	0.15 (0.03, 0.44)	10.89
Gursoy (2005)	→	1.32 (0.69, 2.30)	2.12
Ertekin (2006)	- •	0.55 (0.22, 1.14)	5.09
Akbari (2006)		0.32 (0.15, 0.61)	10.07
Sood (2006)	-	0.32 (0.18, 0.54)	11.54
Saberi-Firouzi (2008)	•	0.14 (0.02, 0.50)	9.76
Demerciken (2008)	↓ •	0.80 (0.35, 1.57)	3.34
Israeli (2010)	↓ •	0.71 (0.26, 1.53)	3.15
Bahari (2010)	-	0.44 (0.18, 0.90)	6.78
Makharia (2011)		1.08 (0.73, 1.52)	6.11
Dalgic (2011)	•	0.38 (0.30, 0.48)	14.12
Kochhar (2012)		0.56 (0.26, 1.06)	6.01
Dehghani (2013)	-	0.60 (0.27, 1.14)	5.51
Overall (I-squared = 60.7%, p = 0.002)	•	0.46 (0.33, 0.58)	100.00
NOTE: Weights are from random effects an	nalysis		

Prashant Singh, et al, JGH 2016

Summary 3: CeD in Asia



- 50 countries
- 60% of the world's population 4.2 billion
- Two largest countries: China and India
 China: 1.35 Billion
 India: 1.22 Billion

No of patients with CeD in Asia is likely to increase

There is a need to understand the epidemiology of coeliac disease in Asia



CeD: In Future

What are the predictions?



CeD: Essential factors





HLA-DQ2 and/or -DQ8)



Wheat production has increased globally



http://www.grdc.com.au/Research-and-Development/GRDC-Update-Papers/2011/09/~/media/F468B203AFBE4A7FB62A5DFBCD0A730C.gif?w=496&h=349

Wheat consumption (kg) per person per year for countries in the Asia Pacific region



Aquino P, Carrión F, Calvo R. *Selected Wheat Statistics. 2001* Cummins AG, J Gastroenterol Hepatol. 2009





National Health and Nutrition Survey Japan, 2010

Wheat statistics in China (1000mt)



Consumption of wheat is over 100 million metric tons for over 1,370 million people



Per capita annual consumption of wheat Rural households: 59.6kgs Wheat flour in urban households: 12.5 kg

Yuan J, PLoS, 2013

Wheat consumption pattern: China



Yuan J, PLoS, 2013



Change in dietary pattern



- Migration of people from rural to urban area
- Change in traditional eating practices to breads, pasta, pizza and burger



Frequency of HLA-DQ2 in the population of various countries in the Asia–Pacific region

< 5%		5-20%	>20%		
Cook	Islands	China	Australia		
Indon	esia	India	Iran		
Japan		Malaysia	Israel		
Korea		Mongolia	New Zealand		
Nauru		Singapore	Pakistan		
New Caledonia		Sri Lanka	Saudi Arabia		
Papua	New Guinea	Taiwan			
Philip	pines	Thailand			
Samoa		Turkey			
		Vietnam			
	Middleton D. Allele*Frequencies in Worldwide Population				

Cummins AG, J Gastroenterol Hepatol. 2009

HLA DQB1*0201/0202 allele in China



Ethinic minorities



Yuan J, PLoS, 2013



Summary 4 Both the initials reports and presence of predisposing factors highlight that coeliac disease exists in many Asian countries

Barriers



- Believes
- Lack of diagnostic tests
- Very high threshold of suspicion







Awareness about CeD should be increased amongst medical clinicians and patients

Final summary



- CeD is now a GLOBAL disease
 - It affects atleast 0.68% of global population (39-56 million globally)
- Prevalence of the disease has increased over past few decades
- Asia is now coming to the centerstage of CeD
- India presents a unique geographical region, with varying prevalence in North and South, to understand the factors



Acknowledgement



Artistic expression





Sankha Samatha