Viral gastroenteritlere bağlı salgınlar Türkiye ve Dünyada Güncel Durum

Dr.Gülay KORUKLUOĞLU

Türkiye Halk Sağlığı Kurumu

Tanımlar

- **Salgın**

Belirli bir yer (veya populasyonda) ve zamanda, beklenenin üzerinde vakanın görülmesidir.

Salgın Kontrolü

Etkin bir salgın kontrolü aşağıda belirtilen basamakların tamamlanmasıyla sağlanır:

- **Şüpheli vakaların bildirilmesi**
- **Hızlı epidemiyolojik inceleme**
- **Hızlı laboratuvar doğrulaması**
- **Etkin kontrol önlemlerinin alınması**

- Ülkemizde Akut Bağırsak Enfeksiyonu sürveyansı ve mevcut durum….

AKUT BARSAK ENFEKSİYONLARI SÜRVEYANSI

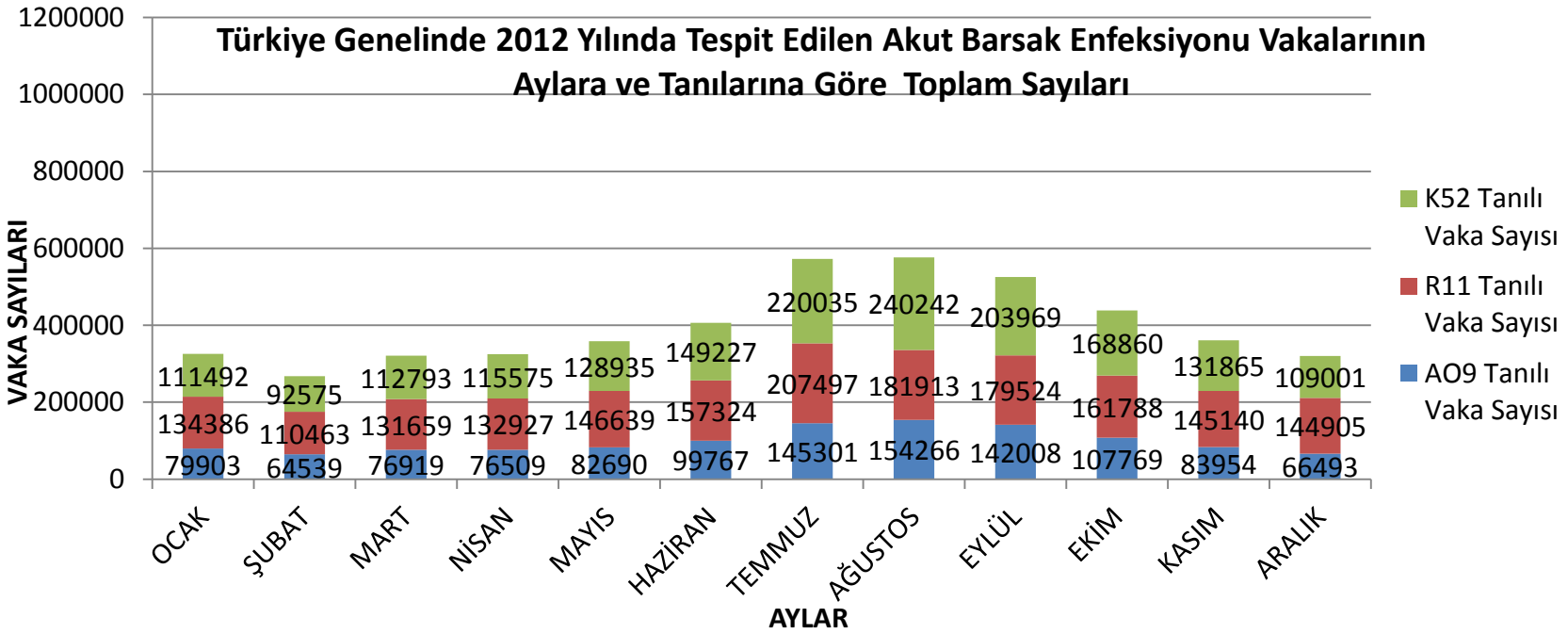
- 2005 yılında mayıs-ekim ayları arasında haftalık sürveyans başlatılmış;
- 2010 yılında tüm yıl, tüm Türkiye'de, günlük sürveyansa geçilmiştir.
- Sürveyansa yıl içinde ara verilmeden,12 ay sürveyansa devam edilmektedir.
- Programın başarısı başta Belediyeler olmak üzere sektörler arası işbirliğine dayanır.
- TSİM(Temel Sağlık İstatistikleri Modülü) üzerinden verilerin günlük takibi yapılmaktadır.

TSİM EKRAN GÖRÜNTÜSÜ

AKUT BARSAK ENFEKSİYONLARI		Tarih
A09; enfeksiyoz kaynaklı olduğu tahmin edilen diyare ve gastro enteritler	0-59 AYLIK	
	5 YAŞ VE ÜZERİ	
	TOPLAM	
R11; bulantı, kusma	0-59 AYLIK	
	5 YAŞ VE ÜZERİ	
	TOPLAM	
K52; enfektif olmayan diğer gastroenterit ve kolit	0-59 AYLIK	
	5 YAŞ VE ÜZERİ	
	TOPLAM	
GAİTA KÜLTÜRÜ SAYISI		
VİBRİO CHOLERAE (A00)		
SALMONELLA SP. (A02)		
SHİGELLA SP. (A03)		
ENTEROHEMORAJİK E. COLİ (A04.3)		
CAMPYLOBACTER (A04.5)		
PARAZİT İNCELEME		
TESPİT EDİLEN ENTAMOEBA HYSTOLİTİCA (A06)		
TESPİT EDİLEN CRYPTOSPORİDİUM (A07.2)		
VİRAL ETKEN İNCELEME		
ROTA VİRUS (A08.0)		
NORO VİRUS (A08.1)		
ADENO VİRUS (A08.2)		
HEPATİT A (B15)		

ABE(AKUT BARSAK ENFEKSİYONU) 2012

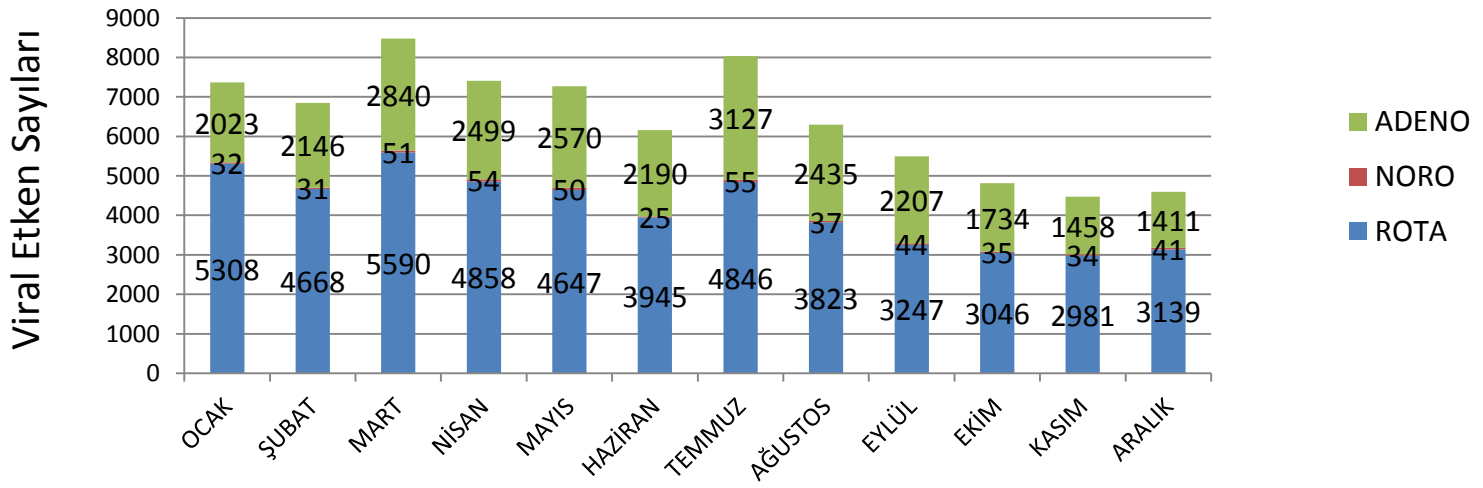
	OCAK	ŞUBAT	MART	NİSAN	MAYIS	HAZİRAN	TEMMUZ	AĞUSTOS	EYLÜL	EKİM	KASIM	ARALIK
AO9 Tanılı Vaka Sayısı	79903	64539	76919	76509	82690	99767	145301	154266	142008	107769	83954	66493
R11 Tanılı Vaka Sayısı	134386	110463	131659	132927	146639	157324	207497	181913	179524	161788	145140	144905
K52 Tanılı Vaka Sayısı	111492	92575	112793	115575	128935	149227	220035	240242	203969	168860	131865	109001



ABE(AKUT BARSAK ENFEKSİYONU)2012VİRAL ETKEN İNCELEMELERİNİN AYLARA DAĞILIMI

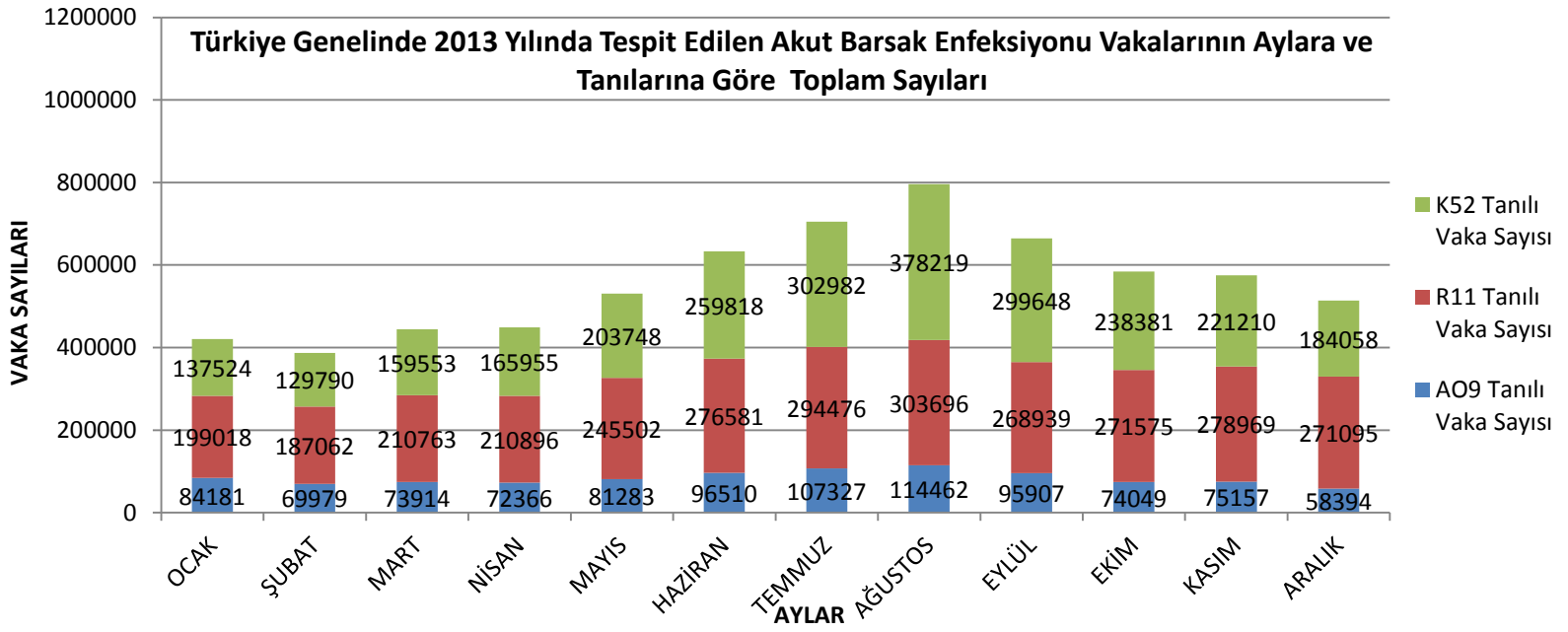
	OCAK	ŞUBAT	MART	NİSAN	MAYIS	HAZİRAN	TEMMUZ	AĞUSTOS	EYLÜL	EKİM	KASIM	ARALIK
ROTA	5308	4668	5590	4858	4647	3945	4846	3823	3247	3046	2981	3139
NORO	32	31	51	54	50	25	55	37	44	35	34	41
ADENO	2023	2146	2840	2499	2570	2190	3127	2435	2207	1734	1458	1411

Türkiye'de 2012 Yılında Tespit Edilen Akut Barsak Enfeksiyonu



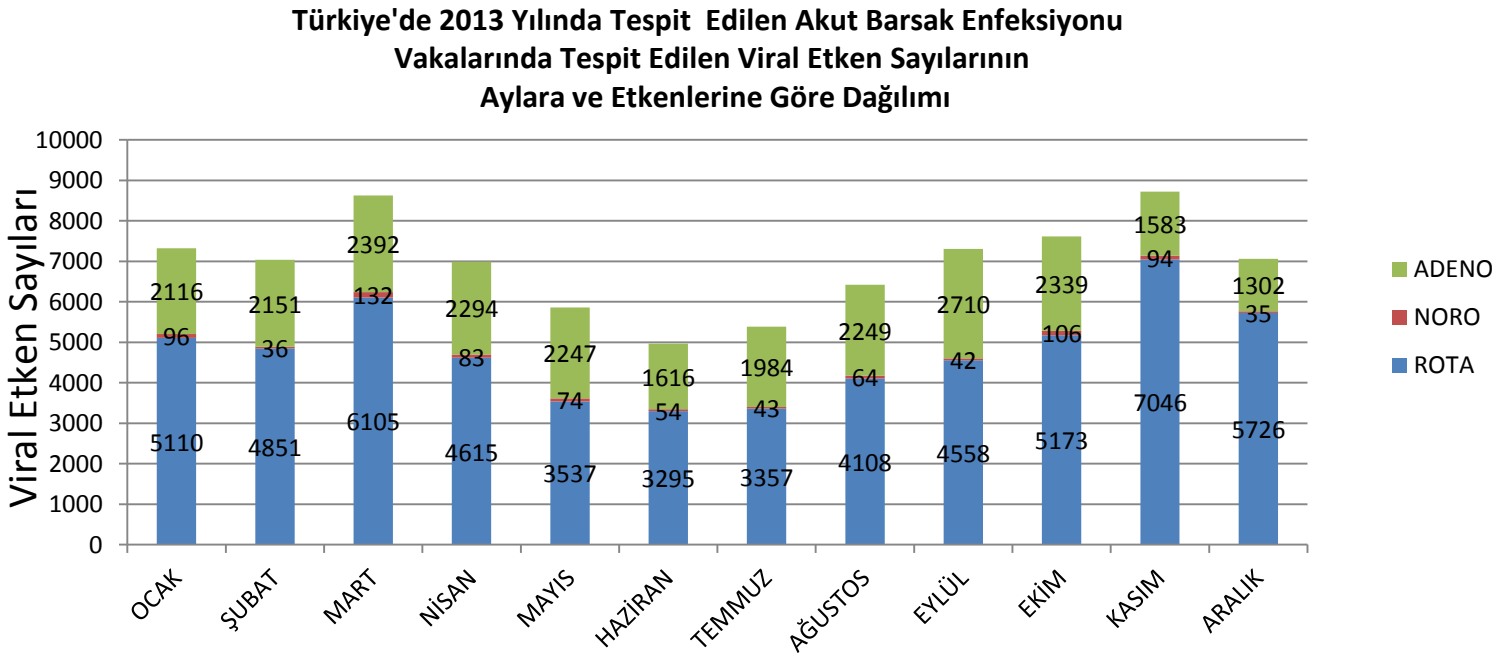
ABE(AKUT BARSAK ENFEKSİYONU) 2013

	OCAK	ŞUBAT	MART	NİSAN	MAYIS	HAZİRAN	TEMMUZ	AĞUSTOS	EYLÜL	EKİM	KASIM	ARALIK
AO9 Tanılı Vaka Sayısı	84181	69979	73914	72366	81283	96510	107327	114462	95907	74049	75157	58394
R11 Tanılı Vaka Sayısı	199018	187062	210763	210896	245502	276581	294476	303696	268939	271575	278969	271095
K52 Tanılı Vaka Sayısı	137524	129790	159553	165955	203748	259818	302982	378219	299648	238381	221210	184058



ABE(AKUT BARSAK ENFEKSİYONU) 2013 VİRAL ETKEN İNCELEMELERİNİN AYLARA DAĞILIMI

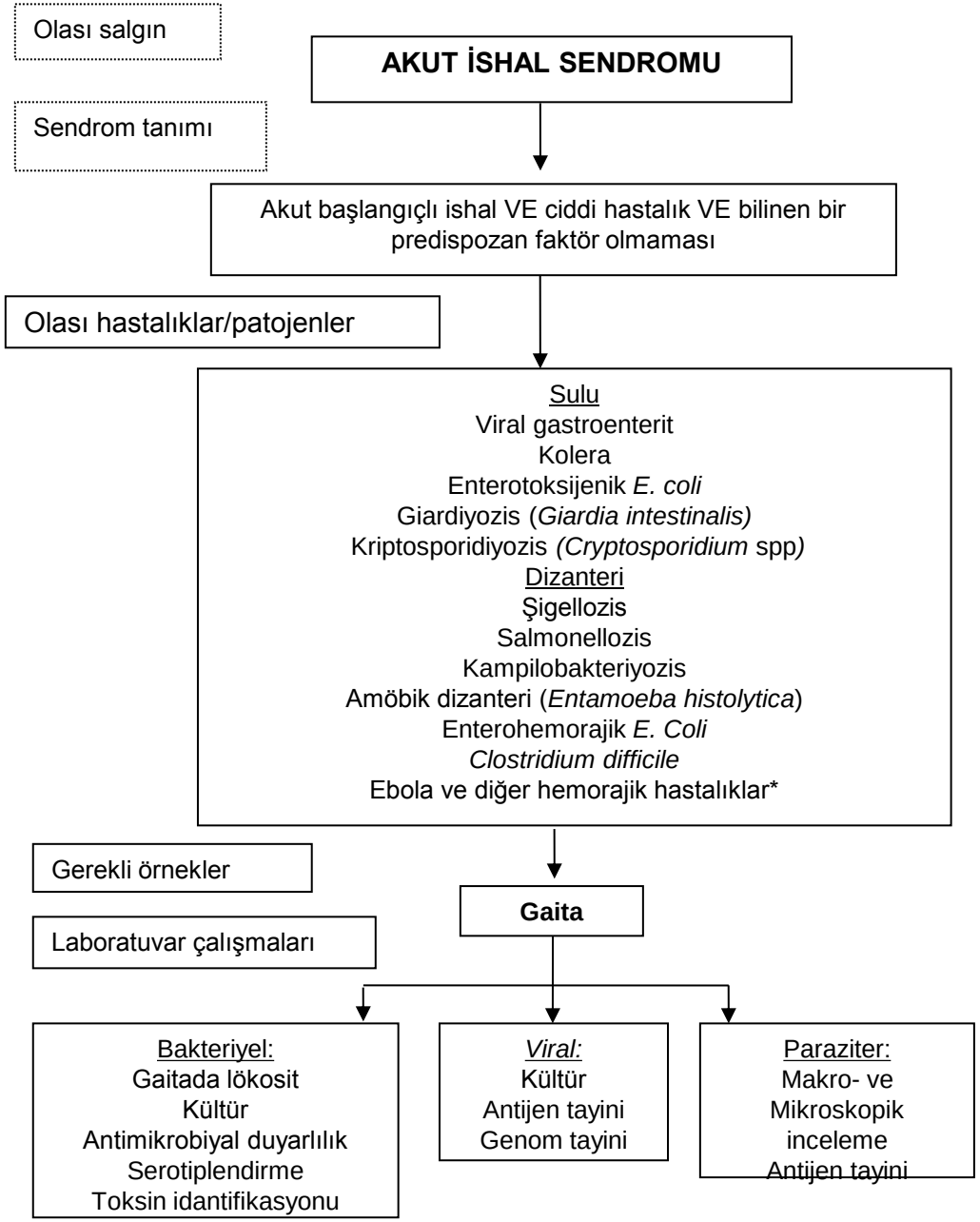
	OCAK	ŞUBAT	MART	NİSAN	MAYIS	HAZİRAN	TEMMUZ	AĞUSTOS	EYLÜL	EKİM	KASIM	ARALIK
ROTA	5110	4851	6105	4615	3537	3295	3357	4108	4558	5173	7046	5726
NORO	96	36	132	83	74	54	43	64	42	106	94	35
ADENO	2116	2151	2392	2294	2247	1616	1984	2249	2710	2339	1583	1302



SU VE BESİN KAYNAKLI SALGINLAR

- **Hedefe Yönelik Stratejiler Nelerdir?**
- Temiz su ve temiz gıdaya erişime ilişkin çalışmalara ağırlık verilecek,
- Yerel yönetimler başta olmak üzere sektörler arası işbirliği güçlendirilecektir.
- Laboratuvara dayalı sürveyans güçlendirilerek vakaların erken tespiti ve salgınların önlenmesi sağlanacak,

- Laboratuvara dayalı surveyans…


Olası salgın
AKUT İSHAL SENDROMU
Sendrom tanımı
Akut başlangıçlı ishal VE ciddi hastalık VE bilinen bir predispozan faktör olmaması
Olası hastalıklar/patojenler
Sulu
Viral gastroenterit
Kolera
Enterotoksijenik E. coli
Giardiyozis (Giardia intestinalis)
Kriptosporidiyozis (Cryptosporidium spp)
Dizanteri
Şigellozis
Salmonellozis
Kampilobakteriyozis
Amöbik dizanteri (Entamoeba histolytica)
Enterohemorajik E. Coli
Clostridium difficile
Ebola ve diğer hemorajik hastalıklar*
Gerekli örnekler
Gaita
Laboratuvar çalışmaları
Bakteriyel:
Gaitada lökosit
Kültür
Antimikrobiyal duyarlılık
Serotiplendirme
Toksin idantifikasyonu
Viral:
Kültür
Antijen tayini
Genom tayini
Paraziter:
Makro- ve
Mikroskopik
inceleme
Antijen tayini

2009-11

- İncelenen örnek sayısı:561
- Viral ajanlar yönünden pozitiflik oranı : %23.7
- Pozitif örneklerin etkene göre dağılımı:

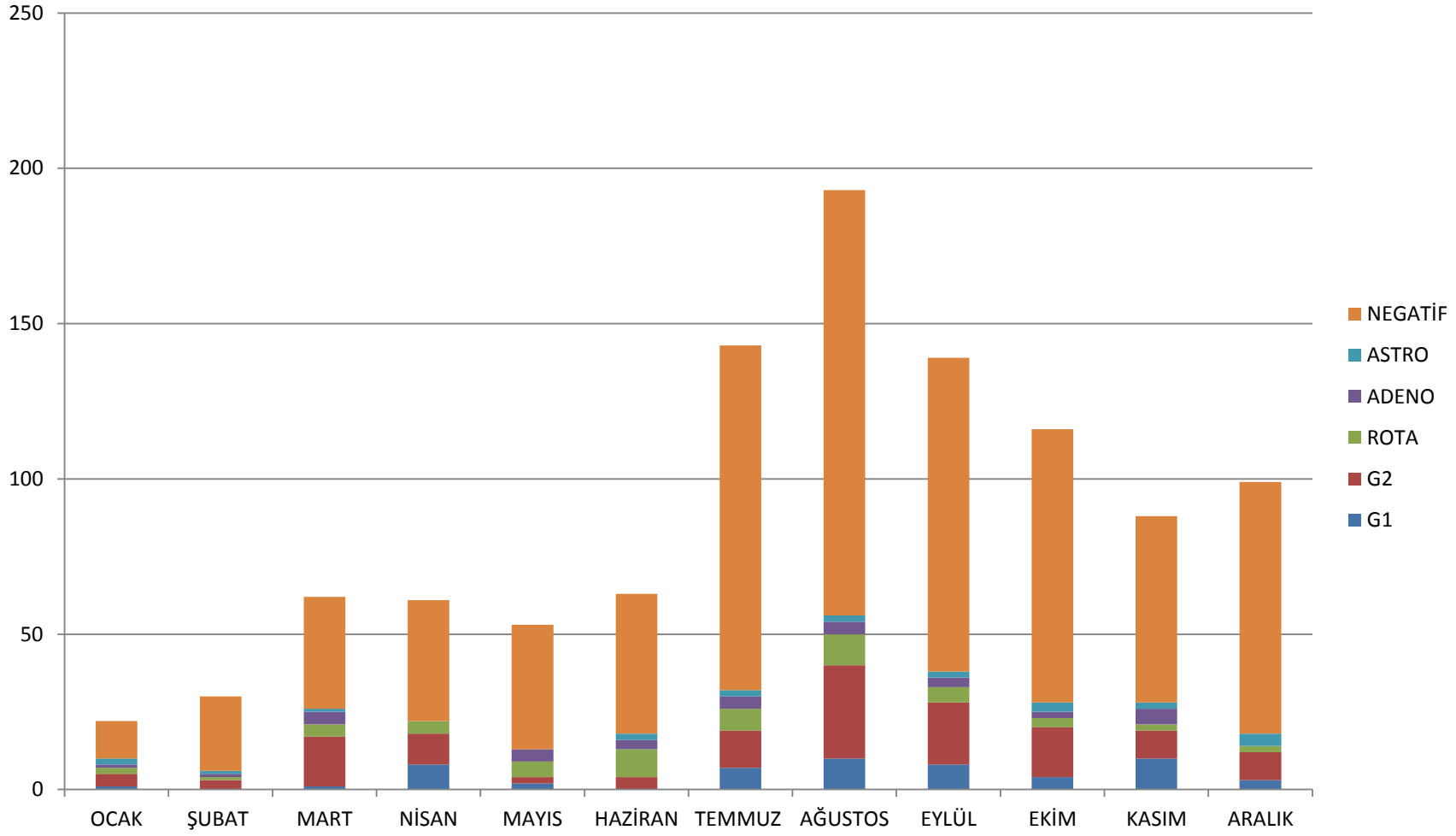
➢ Noro(GI+GII): %57
➢ Rota: %18
➢ Adeno: %6
➢ Astro: %4
➢ Çoklu ajan: %15

2012-14

- İncelenen örnek sayısı:1847
- Viral ajanlar yönünden pozitiflik oranı : %27.4
- Pozitif örneklerin etkene göre dağılımı:

➢ Noro virüs: %58
GI: %28.5 GII:%71.5
➢ Rota: % 18
➢ Adeno: %10
➢ Astro %7
➢ Çoklu ajan: %7

Salgınlarda izole edilen etkenlerin aylara göre dağılımı (2012-2014)



Gerek örnek sayısında, gerekse pozitiflik oranındaki artış, salgın ve örnek yönetimi algoritmasının artan oranda kullanılmaya başlanması ve hasta seçimi/doğru zamanda uygun örnek alınması konusunda sağlık çalışanlarının deneyim kazanması nedeniyle olabileceği düşüncesindeyiz.

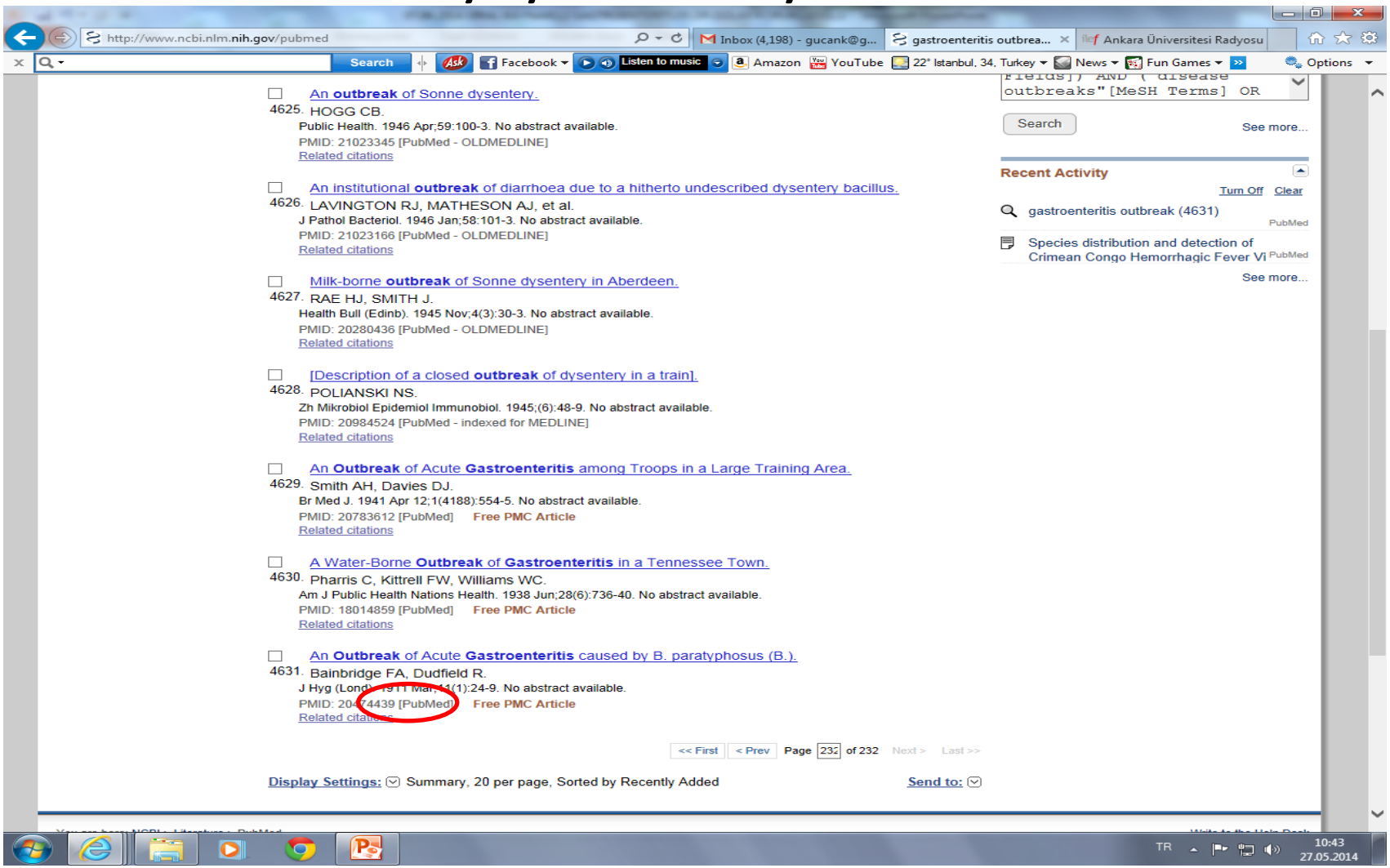
Ancak yine de bu sayıların yeterli olmadığı ve laboratuvara dayalı sürveyansın güçlendirilmesi için daha çok çalışma yapılması gerektiği de açıktır.

- Olası gastroenterit etkenlerinin tanısının hızlı ve doğru olarak yapılması etkin tedavi olanağı sağlayacak, ülkemiz gibi yanlış antibiyotik kullanımının yaygın olduğu bir ülkede gereksiz antibiyotik kullanımını engelleyecek ayrıca antimikrobiyal tedavi gerektiren durumlarda doğru antibiyotik seçimi için yol gösterici olacaktır.

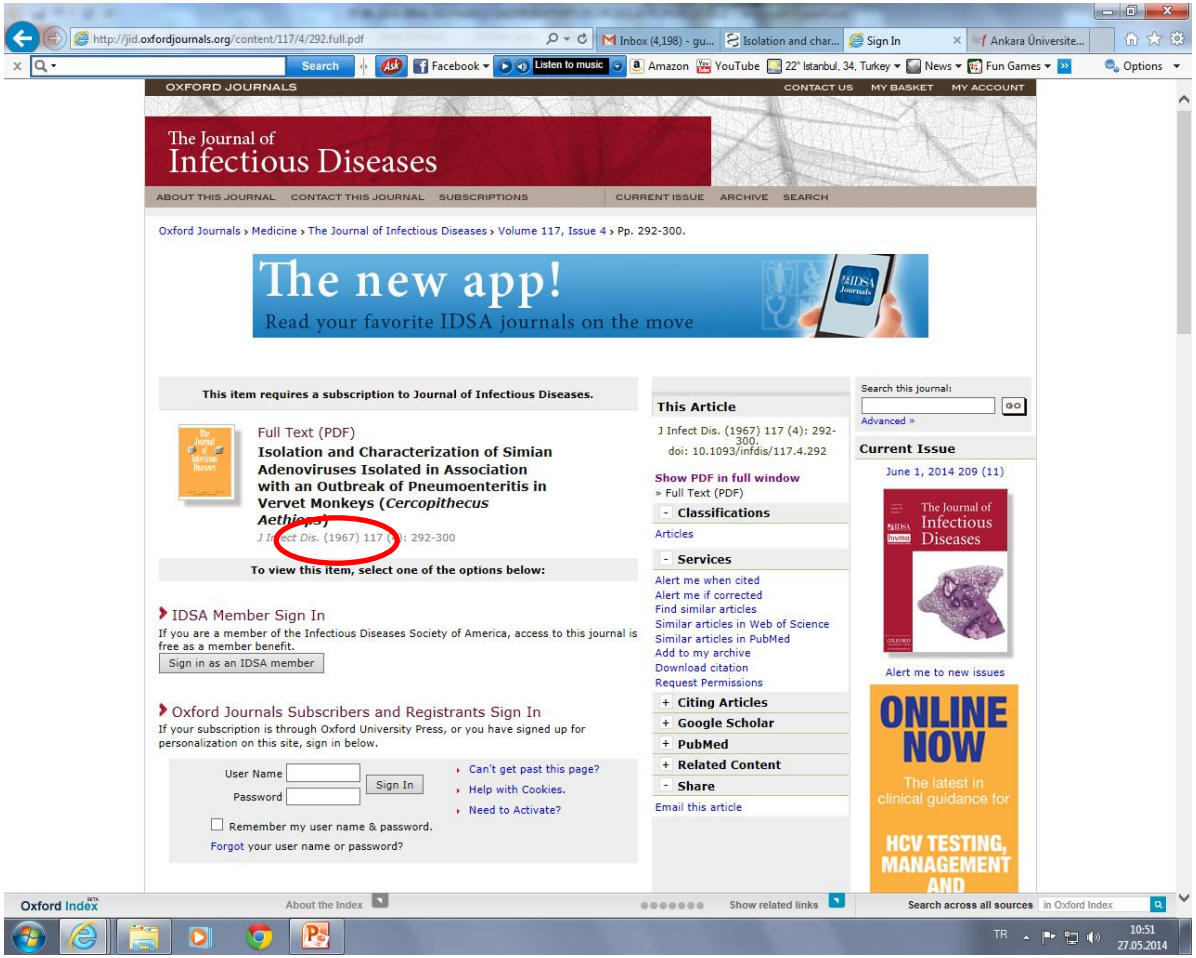
Kontrol önlemlerinin alınması ile akut gastroenterit salgınlarını önlemek böylece hastalığa bağlı sağlık harcamalarını azaltarak ve işgücü kaybını önleyerek hastalık yükünü azaltmak mümkün olmaktadır.

- Dünyada Güncel Durum…

ABE salgınları ile ilgili 4631 yayın…
ilk yayın 1911 yılından..



Viral kaynaklı ilk salgın araştırması 1967 yılından…



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1. Predominance of rotavirus G1[P8] genotype among under-five children with **gastroenteritis** in Mwanza, Tanzania.
Hokororo A, Kidenya BR, Seni J, Mapaseka S, Mphahlele J, Mshana SE.
J Trop Pediatr. 2014 May 24. pii: fmu028. [Epub ahead of print]
PMID: 24859323 [PubMed - as supplied by publisher]

2. A duplex recombinant **viral** nucleoprotein microbead immunoassay for simultaneous detection of seroresponses to human respiratory syncytial virus and metapneumovirus infections.
Zhang Y, Brooks WA, Goswami D, Rahman M, Luby SP, Erdman DD.
J Virol Methods. 2014 May 22. pii: S0166-0934(14)00196-7. doi: 10.1016/j.jviromet.2014.05.008. [Epub ahead of print]
PMID: 24859050 [PubMed - as supplied by publisher]

3. Predominance of norovirus and sapovirus in nicaragua after implementation of universal rotavirus vaccination.
Bucardo F, Reyes Y, Svensson L, Nordgren J.
PLoS One. 2014 May 21;9(5):e98201. doi: 10.1371/journal.pone.0098201. eCollection 2014.
PMID: 24849288 [PubMed - in process] Free Article
Related citations

4. Whole genome analyses of G1P[8] rotavirus strains from vaccinated and non-vaccinated South African children presenting with diarrhea.
Magagula NB, Esona MD, Nyaga MM, Stucker KM, Halpin RA, Stockwell TB, Seheri ML, Steele AD, Wentworth DE, Mphahlele MJ.
J Med Virol. 2014 May 20. doi: 10.1002/jmv.23971. [Epub ahead of print]
PMID: 24841697 [PubMed - as supplied by publisher]
Related citations

5. Norovirus Outbreaks on Commercial Cruise Ships: A Systematic Review and New Targets for the Public Health Agenda.
Bert F, Scaioli G, Gualano MR, Passi S, Specchia ML, Cadeddu C, Viglianchino C, Siliquini R.
Food Environ Virol. 2014 May 17. [Epub ahead of print]
PMID: 24838574 [PubMed - as supplied by publisher]
Related citations

6. Genetic analyses of norovirus GII.4 variants in Finnish children from 1998 to 2013.
Huhti L, Blazevic V, Puustinen L, Hemming M, Salminen M, Vesikari T.
Infect Genet Evol. 2014 May 13. pii: S1567-1348(14)00162-2. doi: 10.1016/j.meegid.2014.05.003. [Epub ahead of print]
PMID: 24837668 [PubMed - as supplied by publisher]

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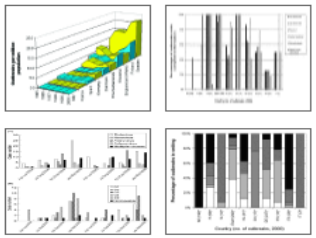

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Oral rehydration for **viral gastroenteritis** in

TR 13:38 27.05.2014

- 1970’li yıllardan önce gastroenterit ataklarının %80’ inin etyolojik tanısı yapılamamaktaydı. Ancak özellikle son yıllarda tanısal mikrobiyoloji alanında ortaya çıkan yeni yöntemler gastroenterit salgınlarının etyolojisinin tanımlanmasında, herbir ajanın oynadığı rolün belirlenmesinde, farklı geçiş yollarının saptanmasında ve kontrol yöntemlerinin belirlenmesinde ciddi kazanımlar sağlanmasına neden olmuştur.
- Tanısal kapasitedeki bu artışa bağlı olarak dünyada yapılan salgın incelemelerinin sayısı giderek artmış ve enfeksiyöz ishallerde virüslerin % 30-70’lere varan oranlarla ilk sırayı aldıkları bildirmiştir.


Yayınlanan araştımaların yıllara göre sayısı
100
90
80
70
60
50
40
30
20
10
0
1967
SAYI

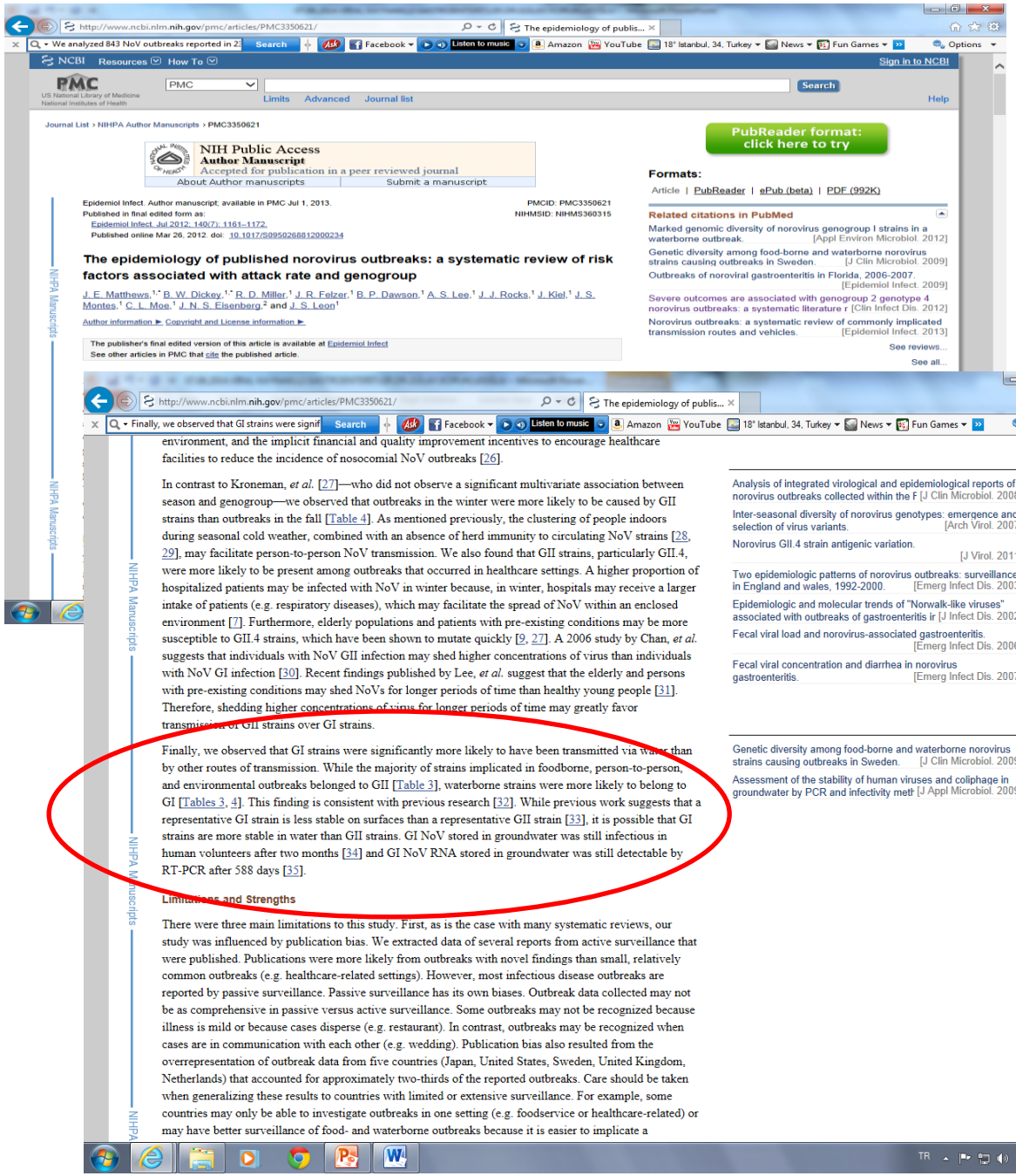
Özellikle son yıllarda moleküler yöntemlerin yaygınlaşması nedeniyle tüm dünyadan bildirilen gastroenterit etkeni olarak viral etyolojik ajanlara ait araştırmaların sayısında ciddi bir artış görülmektedir. Dünya genelinde yapılan araştırmalar incelendiğinde, noro virüs ve rota virüs, en sık karşılaşılan enterit etkenleri olarak karşımıza çıkmaktadır ve her iki etkenle ilgili araştırmaların sayısı da giderek artmaktadır.

Ocak 1993 - Haziran2011 tarihleri arasında yapılan 2435 çalışma değerlendirilmiş ve 45 ülkeden toplam 843 salgının analizi yapılmış ve sonuç olarak; norovirus enfeksiyonu nedeniyle

- 71.724 hasta, 501 hospitalizasyon ve 45 ölüm
- GII.4 genogrubunun daha yüksek oranda hospitalizasyona ve mortaliteye neden olduğu belirlenmiş.

Aynı grup tarafından yapılan ve norovirus kaynaklı 902 salgının epidemiyolojik analizinde ;

- Su kaynaklı salgınların çoğunlukla genogrup GI,
- Gıda kaynaklı ve insandan insana temas yoluyla gelişen salgınların ise daha çok genogrup GII ile meydana geldiği saptanmış..
- Bu durum genogrup GI'in genogrup GII'ye oranla yüzeylerde daha az stabil olması ancak suda uzun süre stabil olarak bulunması ile açıklanmış. Gönüllülerle yapılan bir çalışmada GI'in yeraltı sularında 2 ay süreyle enfeksiyöz olduğu ve 588 güne kadar GI-RNA'nın RT-PCR ile pozitif bulunabildiği gösterilmiş...

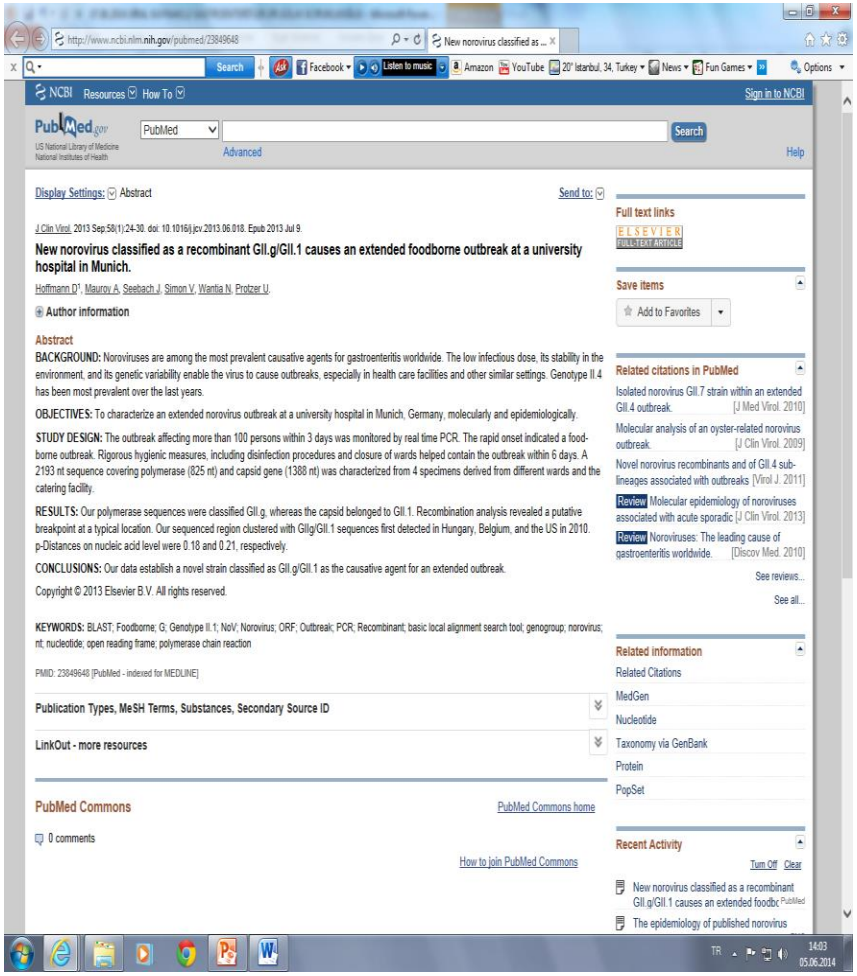


The epidemiology of published norovirus outbreaks: a systematic review of risk factors associated with attack rate and genogroup

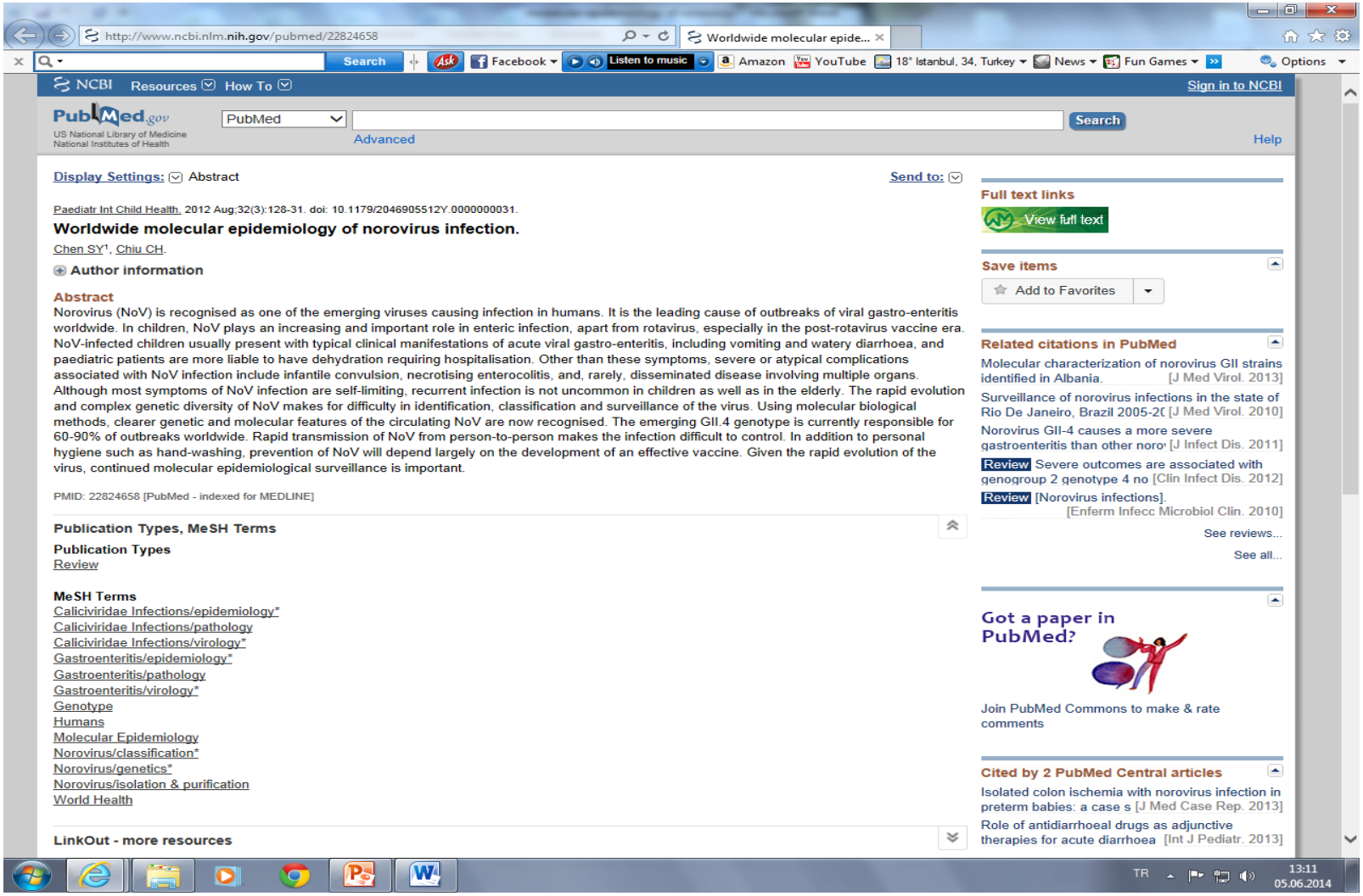
Finally, we observed that GI strains were significantly more likely to have been transmitted via water than by other routes of transmission. While the majority of strains implicated in foodborne, person-to-person, and environmental outbreaks belonged to GII [Table 3], waterborne strains were more likely to belong to GI [Tables 3, 4]. This finding is consistent with previous research [32]. While previous work suggests that a representative GI strain is less stable on surfaces than a representative GII strain [33], it is possible that GI strains are more stable in water than GII strains. GI NoV stored in groundwater was still infectious in human volunteers after two months [34] and GI NoV RNA stored in groundwater was still detectable by RT-PCR after 588 days [35].

Çin de yapılan başka bir araştırmada genotip GII.4 ile birlikte GII.3 de çocuklarda predominant olarak bulunmuştur. Geliştirilecek olan norovirus aşısının mutlaka bu iki kapsid proteinine karşı immunizasyon sağlaması gerektiği vurgulanmıştır.

Almanya'da yapılan gıda kaynaklı başka bir araştırmada da genogrup GII varyantları tanımlanmıştır; GII.g/GII.1



Norovirus enfeksiyonları özellikle çocukluk çağında rota virus aşılama programlarında sonra artan bir enfeksiyon yüküne neden olmaktadır



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Worldwide molecular epide...

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Paediatr Int Child Health. 2012 Aug;32(3):128-31. doi: 10.1179/2046905512Y.0000000031.

Worldwide molecular epidemiology of norovirus infection.

Chen SY[1], Chiu CH.

Author information

Abstract

Norovirus (NoV) is recognised as one of the emerging viruses causing infection in humans. It is the leading cause of outbreaks of viral gastro-enteritis worldwide. In children, NoV plays an increasing and important role in enteric infection, apart from rotavirus, especially in the post-rotavirus vaccine era. NoV-infected children usually present with typical clinical manifestations of acute viral gastro-enteritis, including vomiting and watery diarrhoea, and paediatric patients are more liable to have dehydration requiring hospitalisation. Other than these symptoms, severe or atypical complications associated with NoV infection include infantile convulsion, necrotising enterocolitis, and, rarely, disseminated disease involving multiple organs. Although most symptoms of NoV infection are self-limiting, recurrent infection is not uncommon in children as well as in the elderly. The rapid evolution and complex genetic diversity of NoV makes for difficulty in identification, classification and surveillance of the virus. Using molecular biological methods, clearer genetic and molecular features of the circulating NoV are now recognised. The emerging GII.4 genotype is currently responsible for 60-90% of outbreaks worldwide. Rapid transmission of NoV from person-to-person makes the infection difficult to control. In addition to personal hygiene such as hand-washing, prevention of NoV will depend largely on the development of an effective vaccine. Given the rapid evolution of the virus, continued molecular epidemiological surveillance is important.

PMID: 22824658 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms

Publication Types
Review

MeSH Terms
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Caliciviridae Infections/pathology
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Genotype
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Surveillance of norovirus infections in the state of Rio De Janeiro, Brazil 2005-2([J Med Virol. 2010]
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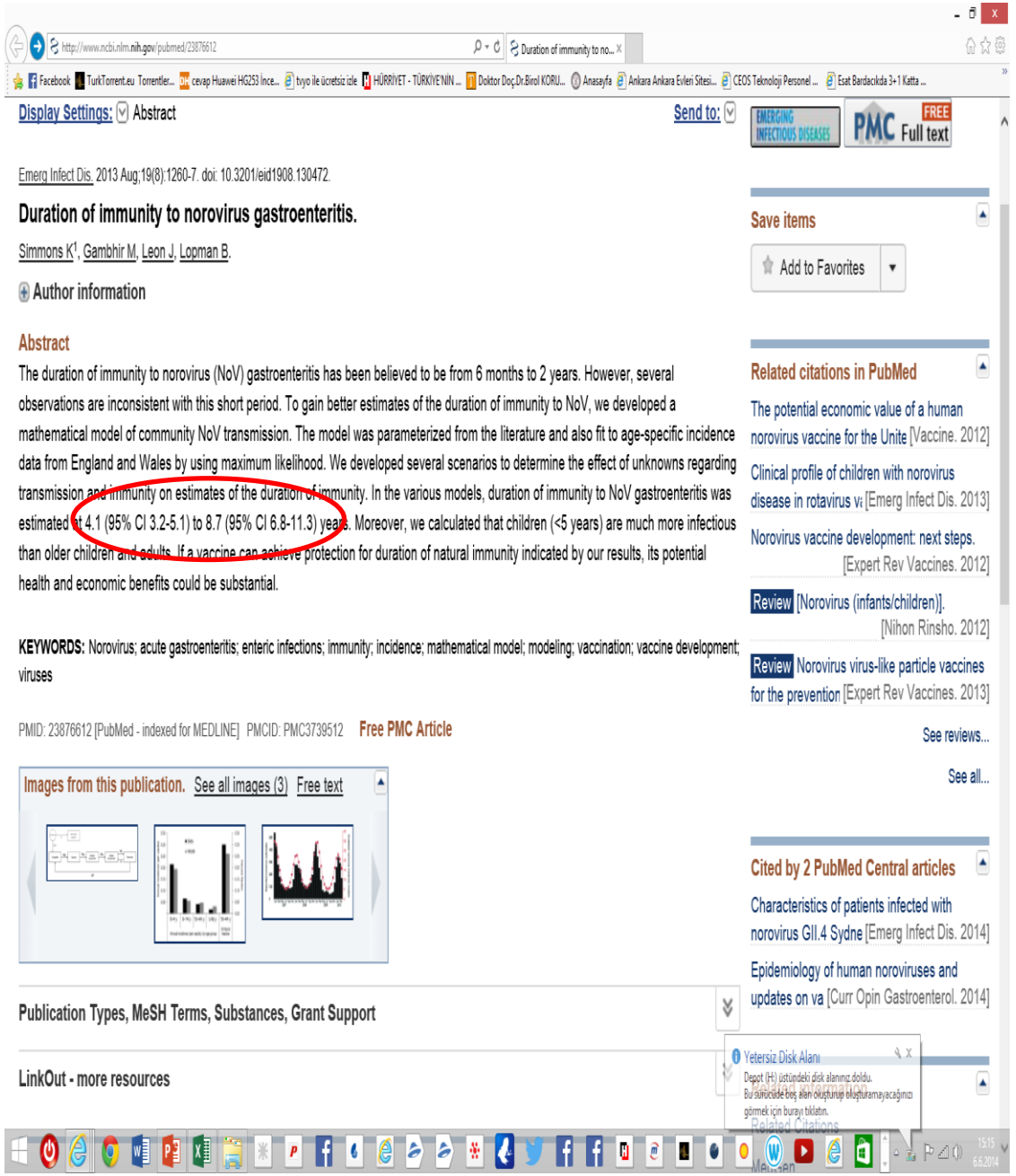
Role of antidiarrhoeal drugs as adjunctive therapies for acute diarrhoea [Int J Pediatr. 2013]

TR 13:11 05.06.2014

- NoV e karşı oluşan bağışıklık süresini araştırmak için yapılan bir çalışmada bu sürenin 4.1 ile 8.7 yıl arasında değiştiği ayrıca 5 yaş altı çocukların daha büyük yaş gruplarına göre daha fazla enfeksiyöz olduğu belirlenmiş..



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Emerg Infect Dis. 2013 Aug;19(8):1260-7. doi: 10.3201/eid1908.130472.

Duration of immunity to norovirus gastroenteritis.

Simmons K[1], Gambhir M, Leon J, Lopman B.

Author information

Abstract

The duration of immunity to norovirus (NoV) gastroenteritis has been believed to be from 6 months to 2 years. However, several observations are inconsistent with this short period. To gain better estimates of the duration of immunity to NoV, we developed a mathematical model of community NoV transmission. The model was parameterized from the literature and also fit to age-specific incidence data from England and Wales by using maximum likelihood. We developed several scenarios to determine the effect of unknowns regarding transmission and immunity on estimates of the duration of immunity. In the various models, duration of immunity to NoV gastroenteritis was estimated at 4.1 (95% CI 3.2-5.1) to 8.7 (95% CI 6.8-11.3) years. Moreover, we calculated that children (<5 years) are much more infectious than older children and adults. If a vaccine can achieve protection for duration of natural immunity indicated by our results, its potential health and economic benefits could be substantial.

KEYWORDS: Norovirus; acute gastroenteritis; enteric infections; immunity; incidence; mathematical model; modeling; vaccination; vaccine development; viruses

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Bu sürücüde boş alan oluşturup oluşturamayacağınızı görmek için buraya tıklatın.

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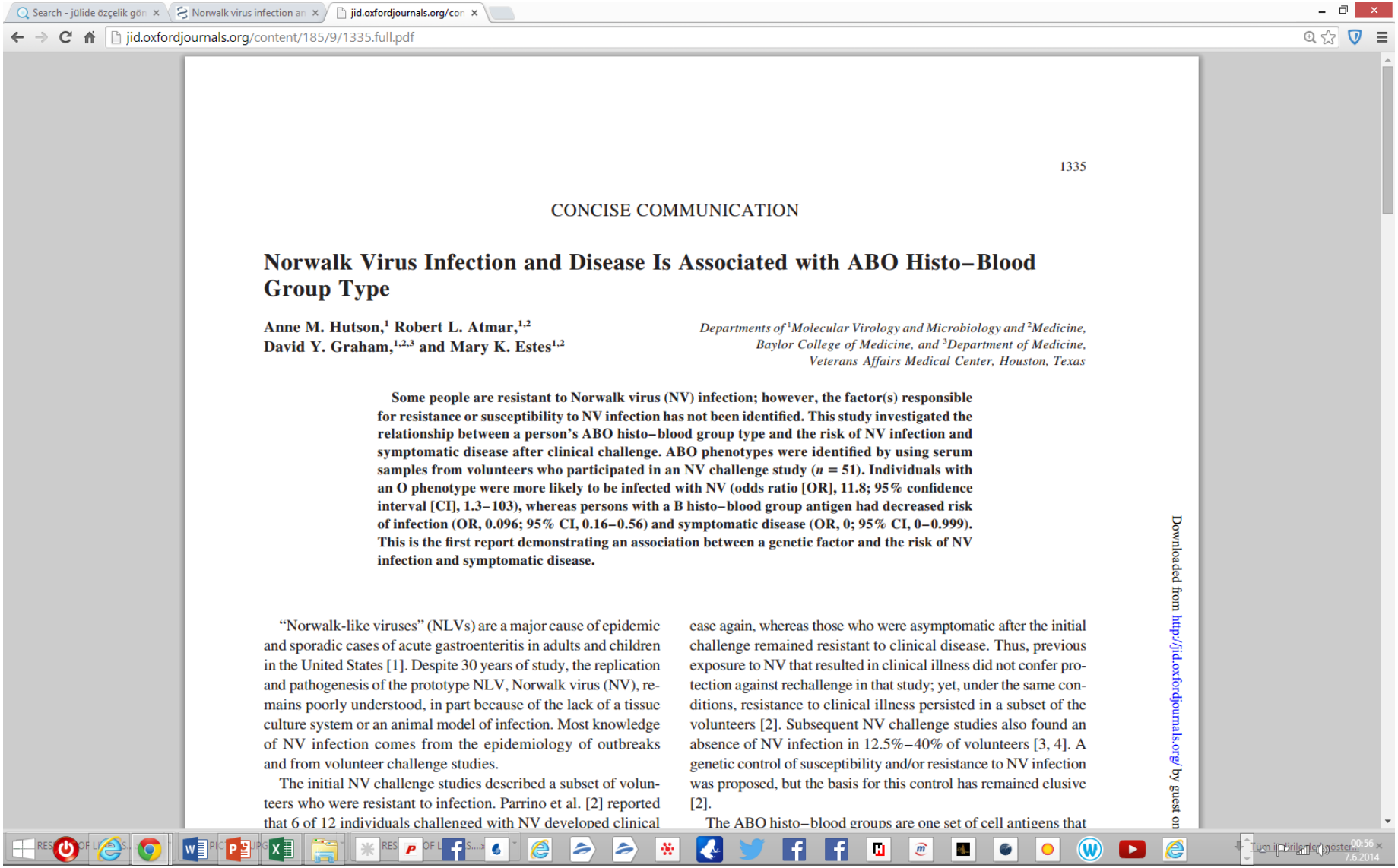

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CONCISE COMMUNICATION

Norwalk Virus Infection and Disease Is Associated with ABO Histo–Blood Group Type

Anne M. Hutson,[1] Robert L. Atmar,[1,2] David Y. Graham,[1,2,3] and Mary K. Estes[1,2]

Departments of [1]Molecular Virology and Microbiology and [2]Medicine, Baylor College of Medicine, and [3]Department of Medicine, Veterans Affairs Medical Center, Houston, Texas

Some people are resistant to Norwalk virus (NV) infection; however, the factor(s) responsible for resistance or susceptibility to NV infection has not been identified. This study investigated the relationship between a person's ABO histo–blood group type and the risk of NV infection and symptomatic disease after clinical challenge. ABO phenotypes were identified by using serum samples from volunteers who participated in an NV challenge study ($n = 51$). Individuals with an O phenotype were more likely to be infected with NV (odds ratio [OR], 11.8; 95% confidence interval [CI], 1.3–103), whereas persons with a B histo–blood group antigen had decreased risk of infection (OR, 0.096; 95% CI, 0.16–0.56) and symptomatic disease (OR, 0; 95% CI, 0–0.999). This is the first report demonstrating an association between a genetic factor and the risk of NV infection and symptomatic disease.

"Norwalk-like viruses" (NLVs) are a major cause of epidemic and sporadic cases of acute gastroenteritis in adults and children in the United States [1]. Despite 30 years of study, the replication and pathogenesis of the prototype NLV, Norwalk virus (NV), remains poorly understood, in part because of the lack of a tissue culture system or an animal model of infection. Most knowledge of NV infection comes from the epidemiology of outbreaks and from volunteer challenge studies.

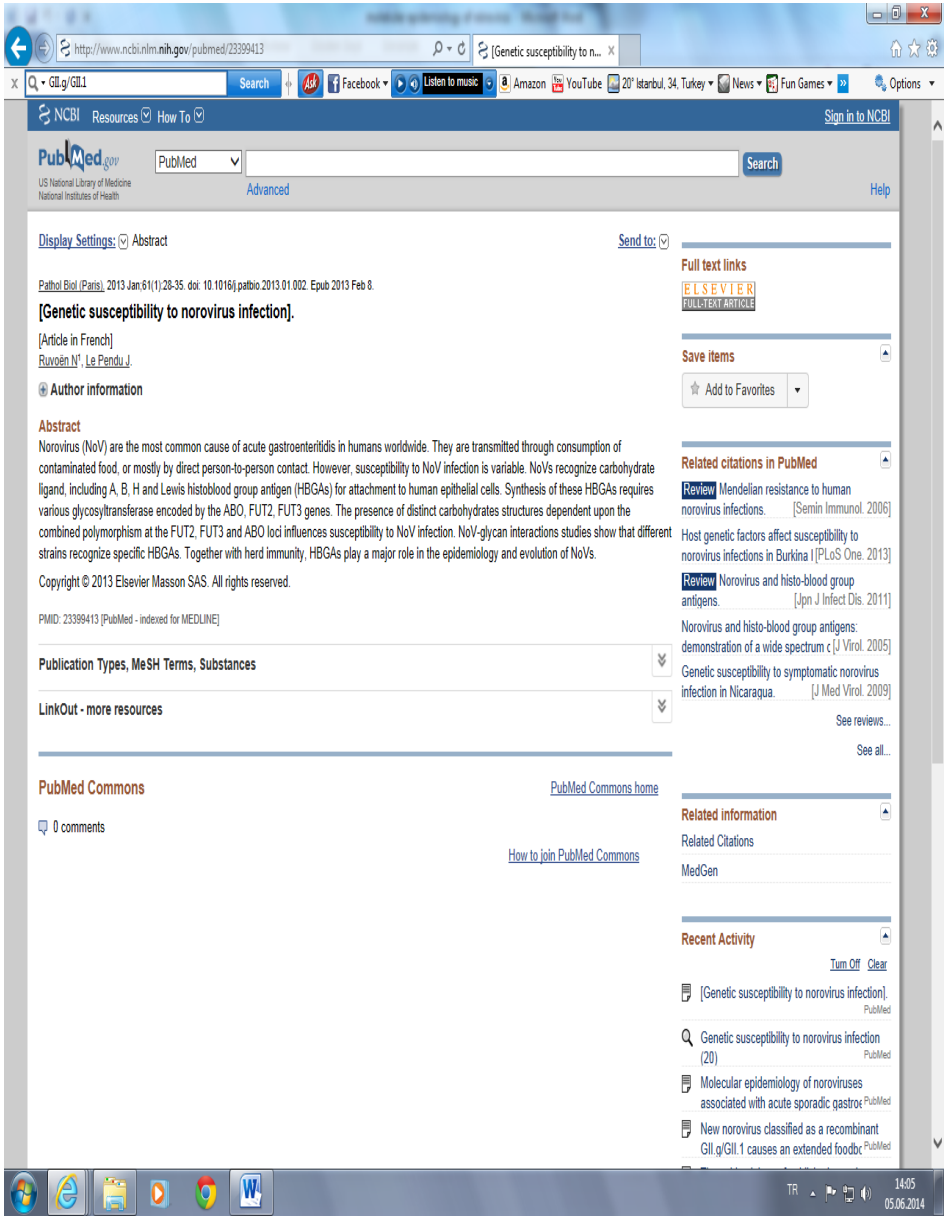
The initial NV challenge studies described a subset of volunteers who were resistant to infection. Parrino et al. [2] reported that 6 of 12 individuals challenged with NV developed clinical disease again, whereas those who were asymptomatic after the initial challenge remained resistant to clinical disease. Thus, previous exposure to NV that resulted in clinical illness did not confer protection against rechallenge in that study; yet, under the same conditions, resistance to clinical illness persisted in a subset of the volunteers [2]. Subsequent NV challenge studies also found an absence of NV infection in 12.5%–40% of volunteers [3, 4]. A genetic control of susceptibility and/or resistance to NV infection was proposed, but the basis for this control has remained elusive [2].

The ABO histo–blood groups are one set of cell antigens that

Genetik duyarlılık

Son olarak 2013 yılında Fransa'da yapılmış bir çalışma göstermiştir ki norovirusun karbonhidrat ligandları tanıması sonucunda insan epitelyal hücrelerine bağlanmasında A,B,H ve Lewis kan grubu antijenleri rol oynamaktadır. NoV'un farklı suşlarının spesifik kan grubu antijenlerini tanıdığı gösterilmiştir.

Bu durum NoV enfeksiyonlarının epidemiyolojisinde anahtar rol oynayacaktır.



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Pathol Biol (Paris). 2013 Jan;61(1):28-35. doi: 10.1016/j.patbio.2013.01.002. Epub 2013 Feb 8.

[Genetic susceptibility to norovirus infection].

[Article in French]

Ruvoën N[1], Le Pendu J.

Author information

Abstract

Norovirus (NoV) are the most common cause of acute gastroenteritidis in humans worldwide. They are transmitted through consumption of contaminated food, or mostly by direct person-to-person contact. However, susceptibility to NoV infection is variable. NoVs recognize carbohydrate ligand, including A, B, H and Lewis histoblood group antigen (HBGAs) for attachment to human epithelial cells. Synthesis of these HBGAs requires various glycosyltransferase encoded by the ABO, FUT2, FUT3 genes. The presence of distinct carbohydrates structures dependent upon the combined polymorphism at the FUT2, FUT3 and ABO loci influences susceptibility to NoV infection. NoV-glycan interactions studies show that different strains recognize specific HBGAs. Together with herd immunity, HBGAs play a major role in the epidemiology and evolution of NoVs.

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TR 14:05 05.06.2014

Hastalık yükü

2014 yılında ABD'de yayınlanan bir araştırmada NGE,RGE ve tüm AGE lerin neden olduğu mali tablonun(hastaneye yatış, hastanede kalma süresinin uzaması, tedavi vb.) 3.88 milyar dolar olduğu ve bu kaynağın enfeksiyon koruma programları için araştırmalarda kullanılmasının halk sağlığına sağlayacağı olumlu katkıya dikkat çekilmiştir..

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Hum Vaccin Immunother. 2014 Apr 14;10(6). [Epub ahead of print]

Burden of acute gastroenteritis, norovirus and rotavirus in a managed care population.

Karve S[1], Krishnarajah G[2], Korsnes JS[1], Cassidy A[3], Candrilli SD[1].

Author information

Abstract

This study assessed and described the episode rate, duration of illness, and health care utilization and costs associated with acute gastroenteritis (AGE), norovirus gastroenteritis (NVGE), and rotavirus gastroenteritis (RVGE) in physician office, emergency department (ED), and inpatient care settings in the United States (US). The retrospective analysis was conducted using an administrative insurance claims database (2006-2011). AGE episode rates were assessed using medical (ICD-9-CM) codes for AGE; whereas a previously published "indirect" method was used in assessing estimated episode rates of NVGE and RVGE. We calculated per-patient, per-episode and total costs incurred in three care settings for the three diseases over five seasons. For each season, we extrapolated the total economic burden associated with the diseases to the US population. The overall AGE episode rate in the physician office care setting declined by 15% during the study period; whereas the AGE episode rate remained stable in the inpatient care setting. AGE-related total costs (inflation-adjusted) per 100 000 plan members increased by 28% during the 2010-2011 season, compared with the 2006-2007 season ($832,849 vs. $1 068 116) primarily due to increase in AGE-related inpatient costs. On average, the duration of illness for NVGE and RVGE was 1 day longer than the duration of illness for AGE (mean: 2 days). Nationally, the average AGE-related estimated total cost was $3.88 billion; NVGE and RVGE each accounted for 7% of this total. The episodes of RVGE among pediatric populations have declined; however, NVGE, RVGE and AGE continue to pose a substantial burden among managed care enrollees. In conclusion, the study further reaffirms that RVGE has continued to decline in pediatric population post-launch of the rotavirus vaccination program and provides RVGE- and NVGE-related costs and utilization estimates which can serve as a resource for researchers and policy makers to conduct cost-effectiveness studies for prevention programs.

KEYWORDS: acute gastroenteritis; duration of illness; health care cost; norovirus; rotavirus

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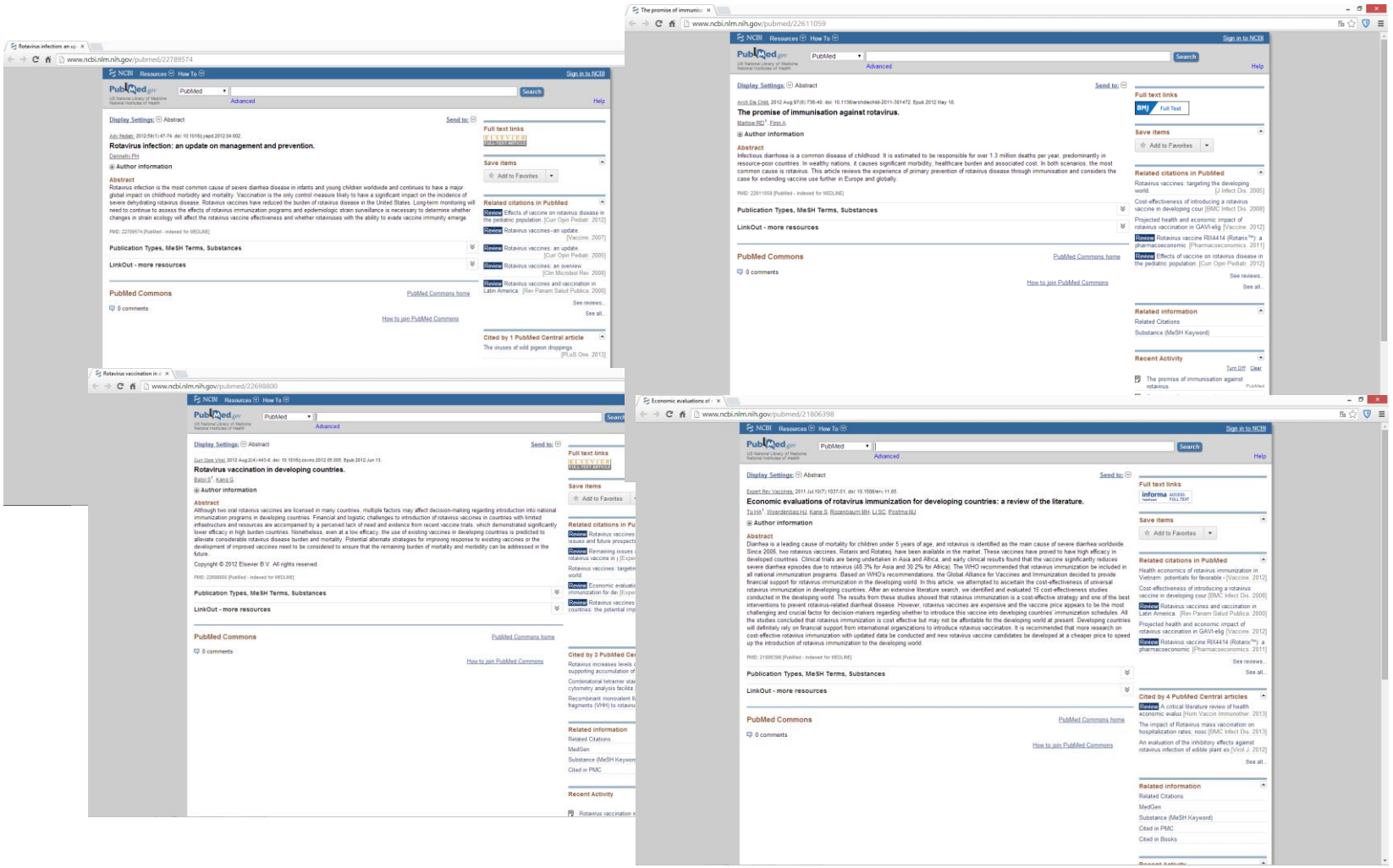
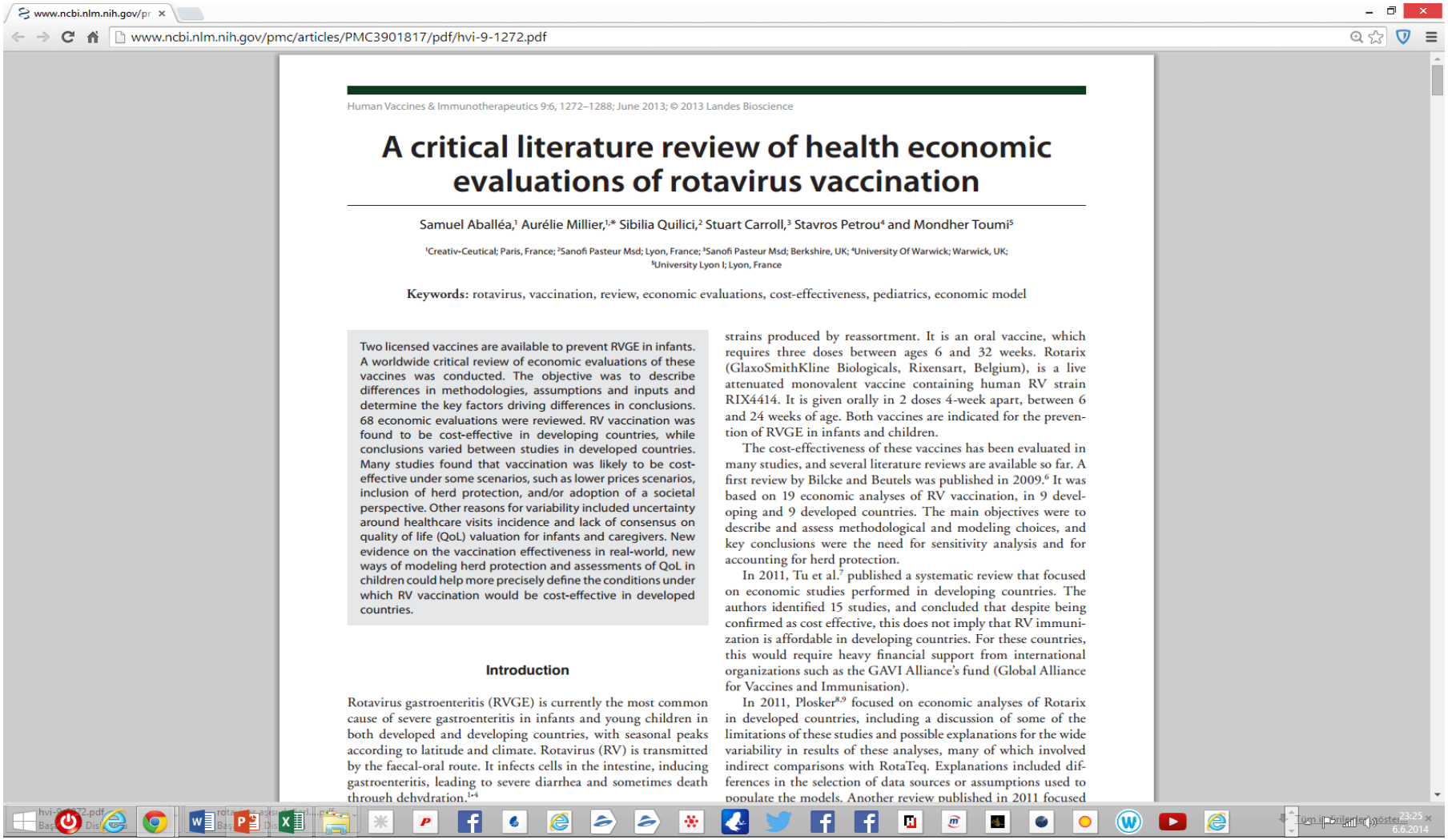
Rotavirüs enfeksiyonlarının özellikle çocukluk çağı ishallerinin ve ishale bağlı ölüm nedenleri arasında ilk sırayı aldığı düşünüldüğünde bu konuda yapılan araştırmaların değeri artmaktadır. Bu konudaki en önemli gelişme ise rotavirüse karşı elde edilen aşıdır ve dünya genelinde bu aşıyla hastalık yükünde ve ölüm oranında ciddi bir düşüş sağlanmıştır. Ancak aşının maliyetinin yüksek olması ve bu nedenle az gelişmiş ülkelerde aşılama programlarının başlatılamamış olması aşıya ulaşılabilirlik konusundaki tartışmaları da beraberinde getirmiştir.

Bu konuda yapılan araştırmaların sayısı her geçen yıl artmaktadır.



Ancak Fransa'da yapılan bir yayında tüm dünyada maliyet/ etkinlik analizi yapan 68 araştırma incelenmiş, her iki aşı da gelişmekte olan ülkelerde maliyet etkin bulunurken gelişmiş ülkelerde toplumsal bağışıklık ve gelişmişlik düzeyiyle artan hayat kalitesi gibi etkenlerden bağımsız olarak kesin bir maliyet etkinlik analizinin yapılamayacağını ortaya koymuştur.



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Human Vaccines & Immunotherapeutics 9:6, 1272–1288; June 2013; © 2013 Landes Bioscience

A critical literature review of health economic evaluations of rotavirus vaccination

Samuel Aballéa,[1] Aurélie Millier,[1,*] Sibilia Quilici,[2] Stuart Carroll,[3] Stavros Petrou[4] and Mondher Toumi[5]

[1]Creativ-Ceutical; Paris, France; [2]Sanofi Pasteur Msd; Lyon, France; [3]Sanofi Pasteur Msd; Berkshire, UK; [4]University Of Warwick; Warwick, UK; [5]University Lyon I; Lyon, France

Keywords: rotavirus, vaccination, review, economic evaluations, cost-effectiveness, pediatrics, economic model

Two licensed vaccines are available to prevent RVGE in infants. A worldwide critical review of economic evaluations of these vaccines was conducted. The objective was to describe differences in methodologies, assumptions and inputs and determine the key factors driving differences in conclusions. 68 economic evaluations were reviewed. RV vaccination was found to be cost-effective in developing countries, while conclusions varied between studies in developed countries. Many studies found that vaccination was likely to be cost-effective under some scenarios, such as lower prices scenarios, inclusion of herd protection, and/or adoption of a societal perspective. Other reasons for variability included uncertainty around healthcare visits incidence and lack of consensus on quality of life (QoL) valuation for infants and caregivers. New evidence on the vaccination effectiveness in real-world, new ways of modeling herd protection and assessments of QoL in children could help more precisely define the conditions under which RV vaccination would be cost-effective in developed countries.

Introduction

Rotavirus gastroenteritis (RVGE) is currently the most common cause of severe gastroenteritis in infants and young children in both developed and developing countries, with seasonal peaks according to latitude and climate. Rotavirus (RV) is transmitted by the faecal-oral route. It infects cells in the intestine, inducing gastroenteritis, leading to severe diarrhea and sometimes death through dehydration.[1-4]

strains produced by reassortment. It is an oral vaccine, which requires three doses between ages 6 and 32 weeks. Rotarix (GlaxoSmithKline Biologicals, Rixensart, Belgium), is a live attenuated monovalent vaccine containing human RV strain RIX4414. It is given orally in 2 doses 4-week apart, between 6 and 24 weeks of age. Both vaccines are indicated for the prevention of RVGE in infants and children.

The cost-effectiveness of these vaccines has been evaluated in many studies, and several literature reviews are available so far. A first review by Bilcke and Beutels was published in 2009.[6] It was based on 19 economic analyses of RV vaccination, in 9 developing and 9 developed countries. The main objectives were to describe and assess methodological and modeling choices, and key conclusions were the need for sensitivity analysis and for accounting for herd protection.

In 2011, Tu et al.[7] published a systematic review that focused on economic studies performed in developing countries. The authors identified 15 studies, and concluded that despite being confirmed as cost effective, this does not imply that RV immunization is affordable in developing countries. For these countries, this would require heavy financial support from international organizations such as the GAVI Alliance's fund (Global Alliance for Vaccines and Immunisation).

In 2011, Plosker[8,9] focused on economic analyses of Rotarix in developed countries, including a discussion of some of the limitations of these studies and possible explanations for the wide variability in results of these analyses, many of which involved indirect comparisons with RotaTeq. Explanations included differences in the selection of data sources or assumptions used to populate the models. Another review published in 2011 focused

Ayrıca son dönemlerde yapılan immünolojik araştırmalar, rotavirüsün uzun dönem koruyuculuk sağlayan spesifik intestinal IgA salgılanmasına neden olduğunu ve bu durumun diğer virüs spesifik IgA çalışmaları için bir model oluşturabileceğini belirtmektedir. Bu da oral yoldan kullanılabilecek ve maliyeti daha ucuz olan aşıların gündeme gelmesine temel oluşturacaktır.

frontiers in IMMUNOLOGY

REVIEW ARTICLE
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The gastrointestinal frontier: IgA and viruses

Sarah E. Blutt and Margaret E. Conner*

Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX, USA

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e-mail: mconner@bcm.edu

Viral gastroenteritis is one of the leading causes of diseases that kill ~2.2 million people worldwide each year. IgA is one of the major immune effector products present in the gastrointestinal tract yet its im
has been difficult to prove.
models in which pathogene
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systems in which new area
term maintenance of viral-s

Keywords: IgA, rotavirus, calicivir

INTRODUCTION

Gastrointestinal infections kill about 2.2 million people each yea
worldwide (1). In the United States, between 60 and 70 million ar
affected annually with gastrointestinal diseases (2) and viral gas-
troenteritis ranks among the top 15 principal discharge diagnose

and recurrence of gastrointestinal viral infections. In fact, it is estimated that 85–90% of IgA-deficient individuals are asymptomatic (25). One explanation might be that individuals with low levels of serum IgA may actually have sufficient secretory IgA at their mucosal surfaces to remain asymptomatic (28, 29). Another might be that other antibody isotypes, particular IgM, via transport to the mucosal surface, compensates for the loss of IgA (30–32).

IgA AND PROTECTIVE IMMUNITY AGAINST GASTROINTESTINAL VIRAL INFECTIONS

Since IgA is produced in large quantities at mucosal surfaces including the gastrointestinal tract, it has long been presumed that IgA is a critical factor in protection of these surfaces against viral infections. Many studies in humans correlate increases in viral-specific IgA levels at the mucosal surface with either the cessation of virus excretion or protection against infection and disease (33–37). With the lack of an overt clinical profile in IgA-deficient humans, it has been difficult to discern the importance of IgA in the immune response to gastrointestinal viruses. Adding to this difficulty are the relatively few animal models of enteropathogenic or non-enteropathogenic gastrointestinal virus infections in which the pathogenesis and immune response, including IgA induction to the virus, faithfully models infection in humans. There are several reasons for the lack of robust animal models. Several of the common enteropathogenic and non-enteropathogenic viruses only replicate in humans or primates, limiting studies that can be performed to determine IgA importance (38). Other viruses infect

Table 1 | Role of IgA in protective from non-enteropathogenic and pathogenic intestinal viral infections.

Virus	IgA			
	Induced by infection (natural/exp)	Correlate of protection		Required for protection
		Humans	Animals	
NON-ENTEROPATHOGENIC				
Poliovirus	Y	Y	?	?
Coxsackievirus	Y	?	?	?
Echovirus	Y	?	?	?
Hepatitis A	Y	?	?	?
Reovirus	Y	?	Y	Y
HIV	Y	Y/N	Y/N	?
ENTEROPATHOGENIC				
Rotavirus	Y	Y	Y	Y
Calicivirus	Y	Y/N	?	?
Adenovirus	Y	?	?	?
Astrovirus	Y	?	?	?

Y, yes; N, no; ?, unknown.

of memory IgA responses in the intestine. Therefore, whether IgA memory in the intestine to enteric viral pathogens undergoes the

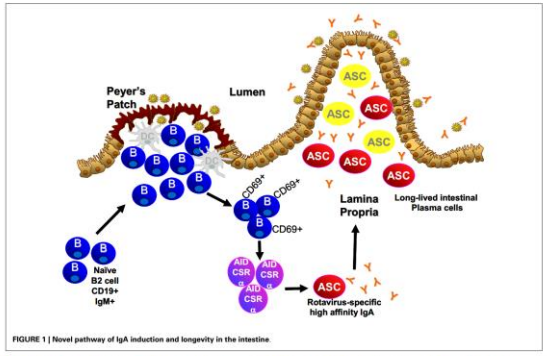

FIGURE 1 | Novel pathway of IgA induction and longevity in the intestine.

Ancak tüm bu araştırmalara rağmen yine de her iki ajanla ve diğerleriyle ilgili olarak salgınlarda ölüm oranlarının ve dünya genelinde hastalık yükünün azaltılması için araştırmaların artarak devam etmesi gerekmektedir.

Teşekkürler…

Viroloji Laboratuvarı

- Tunca Atak
- Hülya Karademirtok
- Nilgün Gökalp
- Songül Özen
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- Ve tüm çalışma arkadaşlarıma….

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