Outcome of Hepatitis E-virus Infection of Egyptian Pregnant Females

by

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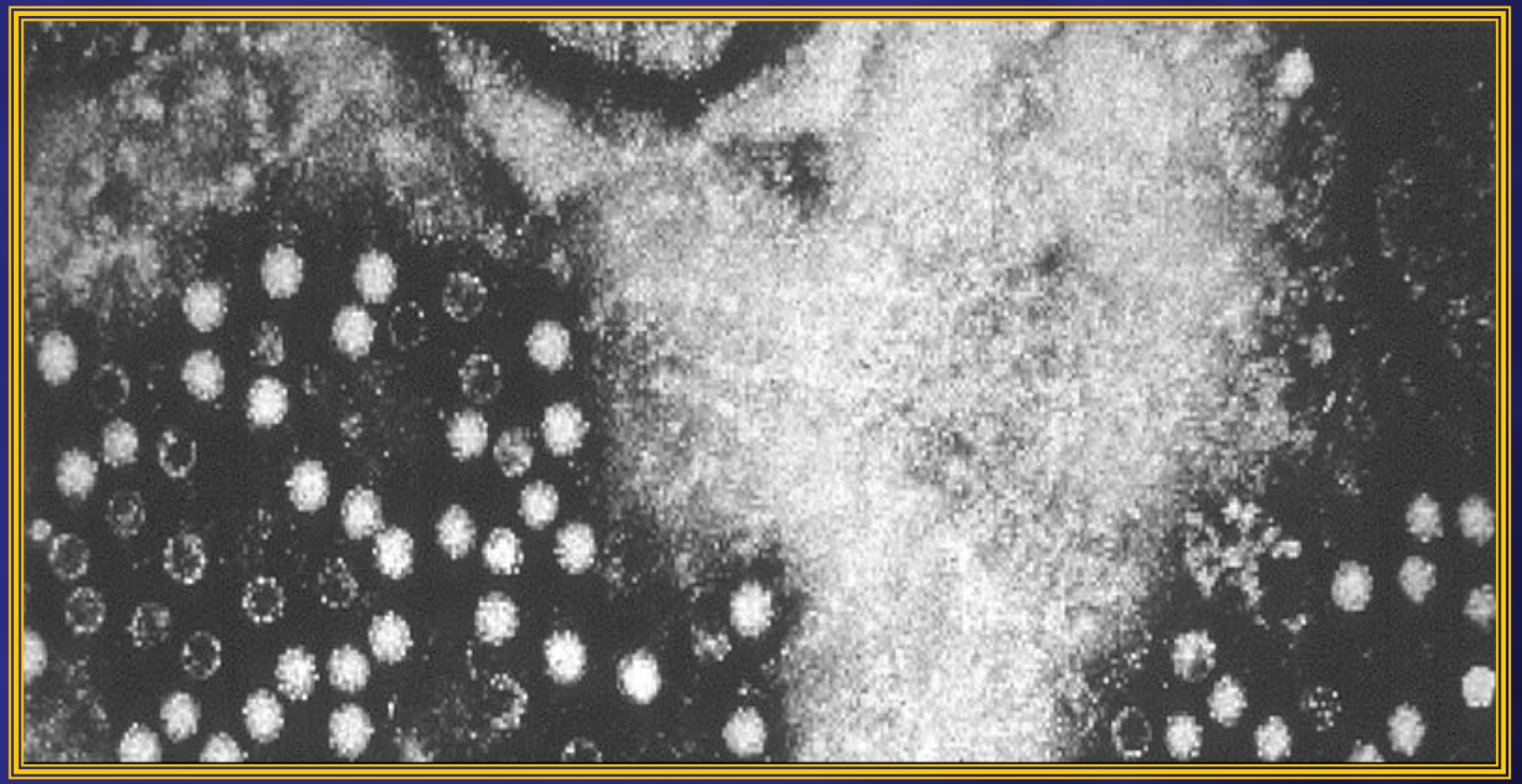
Hepatitis E-virus



Hepatitis E-virus

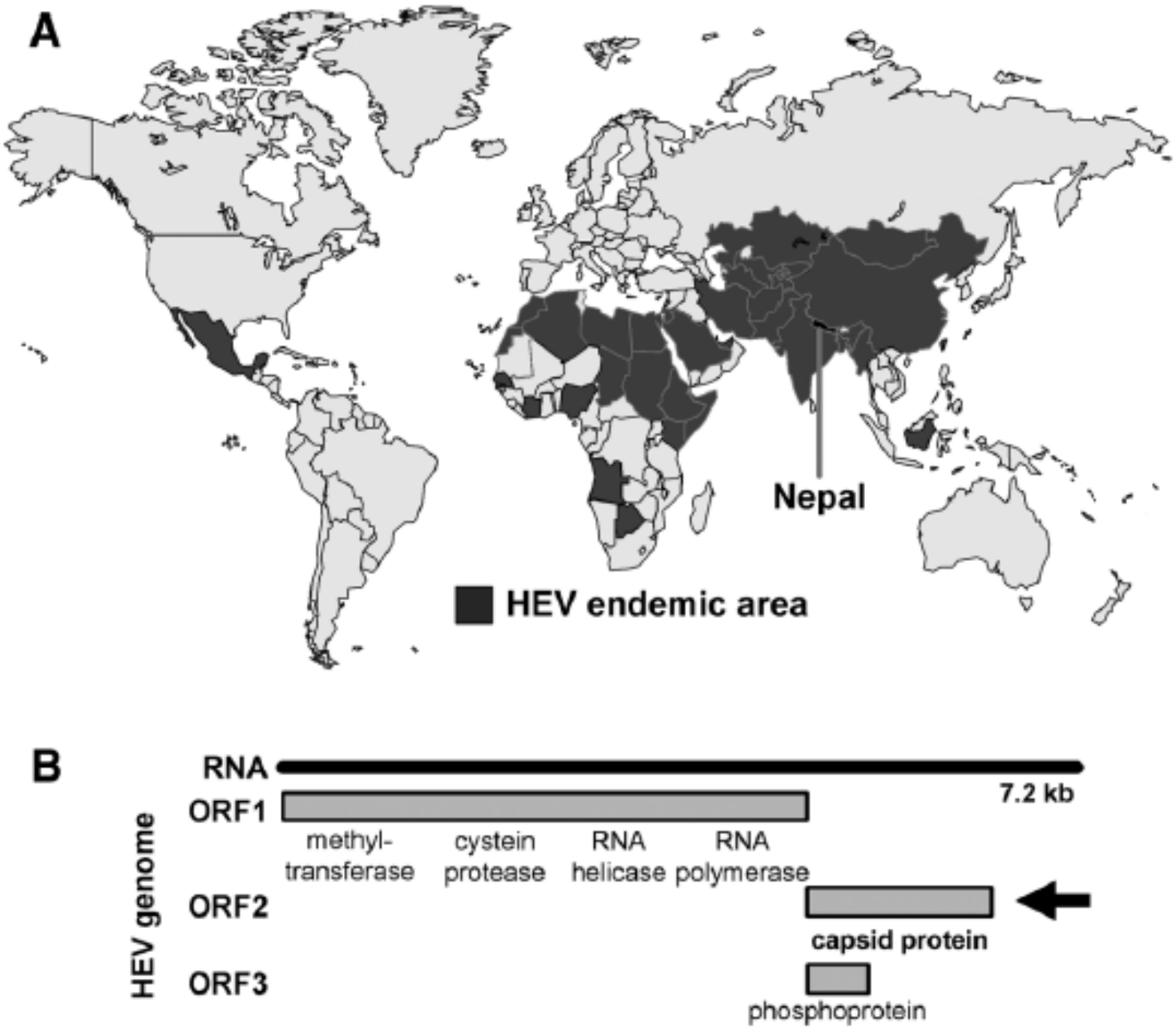
Single stranded RNA virus

- Similar to caliciviruses in structure but may be a separate virus family
- Genome has been cloned and sequenced but virus has not been grown in vitro

Hepatitis E-virus

Epidemiology

- Primarily transmitted by drinking contaminated water
  - Person-to-person transmission uncommon
  - Vertical transmission reported
- Endemic countries include Mexico, Indian subcontinent, southern Russia, SE Asia, and northern and eastern Africa


A
Nepal
HEV endemic area
B
RNA
7.2 kb
ORF1
methyl-
transferase
cystein
protease
RNA
helicase
RNA
polymerase
ORF2
capsid protein
ORF3
phosphoprotein
HEV genome

Hepatitis E-virus

Clinical Features

- Incubation period 40 days (range 15-60)
- Mortality increased in pregnant women (15-25% vs. 0.5-3%)
- Chronic infection in transplantation patients

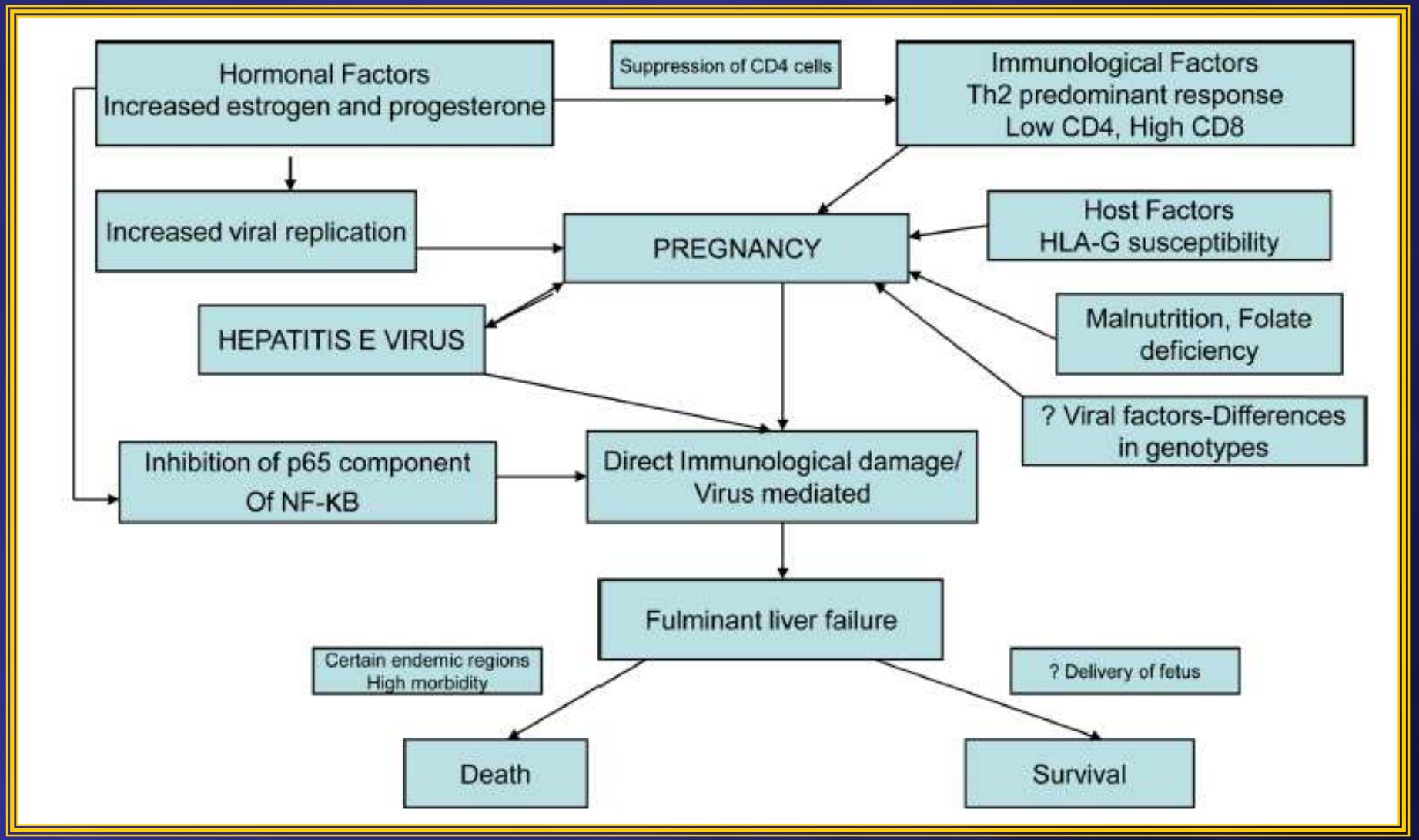
Studies on Hepatitis-E Infection and Pregnancy

Study	Subjects (n)	Prevalence of hepatitis E virus Infection (%)	Prevalence of fulminant liver failure (%)	Mortality Rate (%)
Khuroo et al. (North India)	76	86	69	55
Rasheeda et al. (South India)	115	75	3.4	3.4
Tsega et al. (Ethiopia)	32	59	-	42
Stoszek SK et al. (Egypt)	2428	84.3	0	0

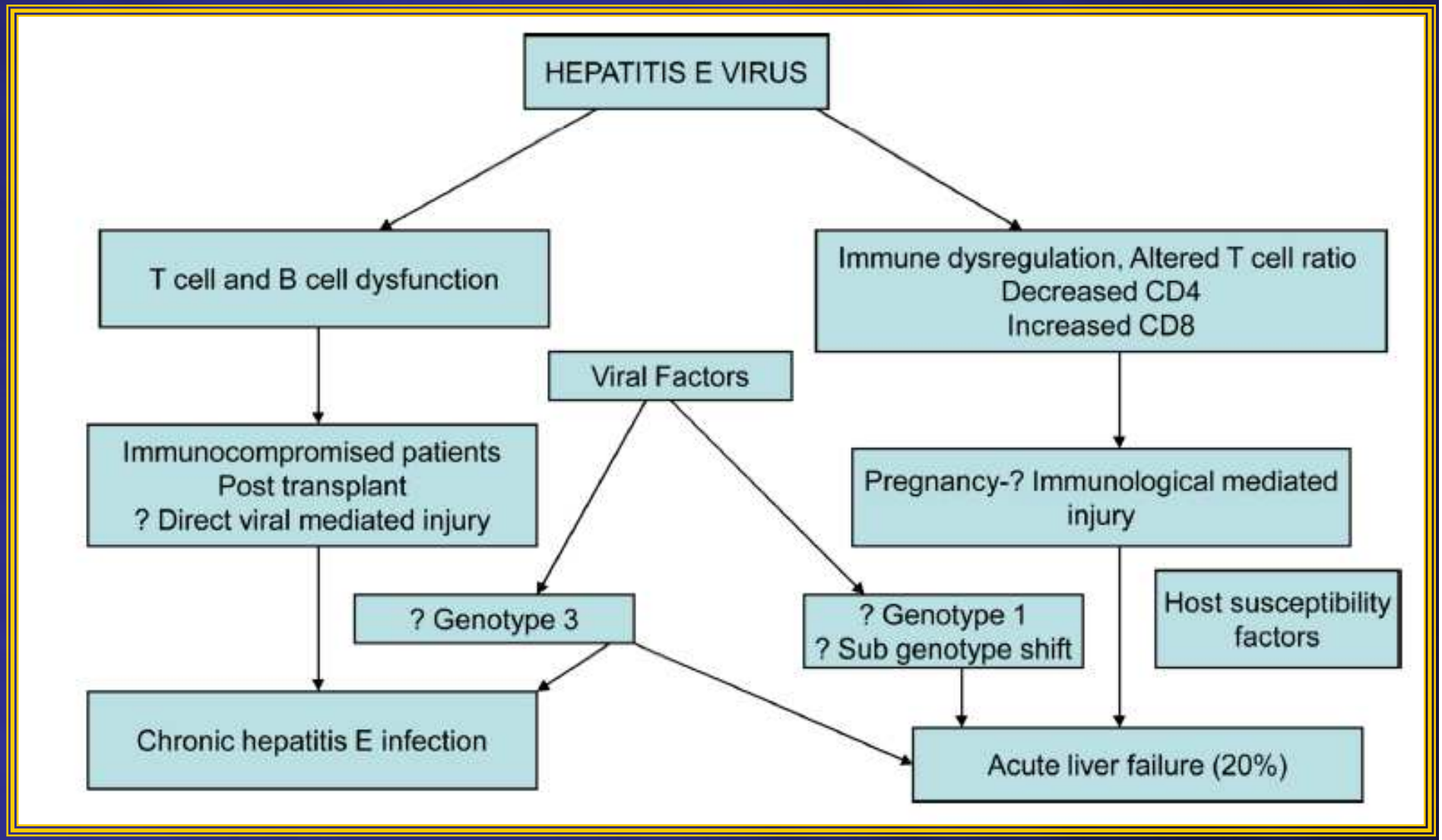
Comparison of Some Features of HEV

	India	Egypt
Source of infection	religious communal water supply & poor sanitation	poor sanitation
Age		
1° infection	adults	children
2° infection	adults	adults
Seroprevalence / age	40% by adulthood	35% childhood
		75-85% adulthood
Fulminant HEV in 3rd trimester pregnancies	20%	Unrecorded
Abortion and/or infant death	20% - 60%	22%

Pathogenesis of HEV in Pregnancy



Probable Hypotheses for the variable pathogenesis of HEV



Materials and Methods

- **Primer for HEV:** Sense and antisense synthetic oligonucleotide primers corresponding to the nucleotide sequence of HEV Putative Polymerase gene in ORF1 (Reyes et al., 1990, 1991).
- Antisense primer (nt. 1117-1135). ET 1.1R15`-CAG GGC CCC CAA GTT CTT CT-3`.
- Sense primer (nt. 717 – 736). ET 1.1 F1 5`-GCT CAT TAT GGA GAG AGT GTG T-3`. The product segment is 381 bp length.
- **Methods:** The protocol described by Reyes et al. (1990) for HEV PCR was followed.
- In house dot ELISA for HEV antigen detection commercial ELISA for IgG anti HEV/IgM anti-HEV.

Comparison of the incidence of IgM or IgG anti-HEV antibody between aborted and full-term delivered women

	Aborted Women		Full-term Delivery Women		P-value
	Frequency	%	Frequency	%	
Anti-HEV IgM +ve	3	2.5	-	none	P>0.05
Anti-HEV IgG +ve	24	20	13	10.83	P<0.05
HEV-RNA +ve	17	70.83	none	none	P<0.01
HEV-RNA -ve	7	29.17	13	100	

HEV Vertical Transmission: correlation of Hepatitis E viremia antigenemia and anti-HEV antibody status of aborted fetal tissue and relevant maternal sera

Sample No.	Maternal Serum				Fetal Tissue	
	HEV-RNA RT-PCR	HEV Ag Dot ELISA	IgM*	IgG*	HEV-RNA PT-PCR	HEV Ag Dot ELISA
Total	17	17	3	24	15	15

Maternal HEV Infection Fetal Transmission Outcome in Egyptian Parturient Mothers Spontaneous Abortion

Mother HEV Markers	Abortion (%)
IgM anti-HEV HEV antigen HEV-RNA	3 (100%)
IgG anti-HEV HEV antigen HEV-RNA	26 (86%)
IgG anti-HEV HEV antigen	4 (12%)
Total abortions/Total pregnancies	33/145 (22.8%)

Conclusion

We present data that indicates inefficiency of maternal protective immunity against acute HEV infection and inability of preexisting anti-HEV IgG to prevent the infection of the fetus in utero. Probable factors are: modulation of maternal immunity mainly cell mediated immune (CMI) responses during pregnancy or the existence of more than one genotype of HEV without cross protection or HEV virulent mutants that escape immune surveillance in Egyptian community of high HEV endemicity. The incidence of 22.8% fetal wastage in maternal HEV infection that we detected exceeds the deleterious effects on the fetus of any TORCH members.


Thank You