P-8

Comorbidities increase In-Hospital Mortality in Dengue Patients in Mexico

TOH M.L.[1], BAURIN N.[1], MORLEY D.[2], RECAMIER V.[2], GUERGOVA-KURAS M.[2], PUENTES-ROSAS E[3], OCHIAI L.[4], COUDEVILLE L.[1], MASCAREÑAS C.[3]

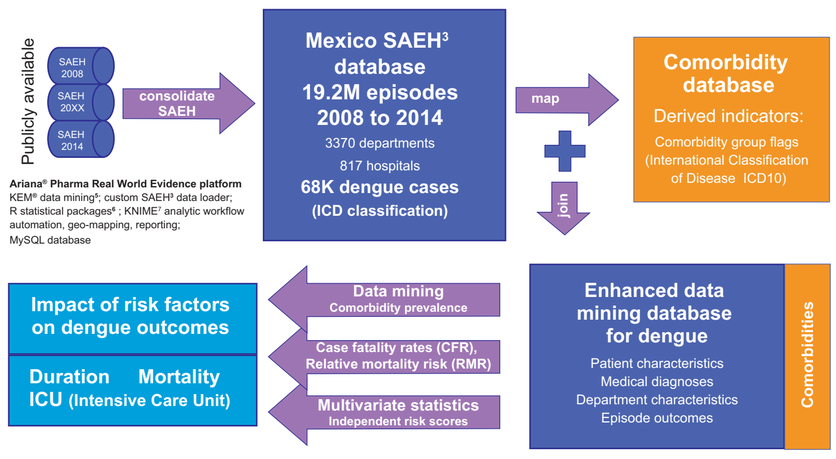
[1]Sanofi Pasteur, France; [2]Ariana Pharma, France; [3]Sanofi Pasteur, Mexico; [4]Sanofi Pasteur, Singapore

BACKGROUND

- Dengue represents an unmet medical and public health issue with more than half the worlds population at risk[1]
- Dengue patients with comorbidities may be at higher risk of death, but there are few large scale studies[2]
- Data mining of hospital databases provides insights on the impact of diseases on the healthcare infrastructure[3-4] and contributes to document the disease burden on public health
- Predictive factors for dengue mortality in high risk populations could aid in determining those that would benefit most from dengue preventative measures

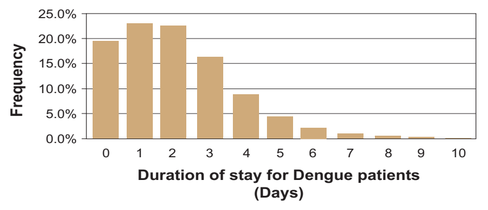
MATERIALS & METHODS

Retrospective analysis of risk factors for dengue mortality in a hospitalized patient database



Modeling the relative impact of comorbidities on dengue patient outcome using risk factors

Measure of patient outcome (cases): ICU, death and duration of stay



	not ICU	ICU
Alive	67,851	76
Dead	259	8

Example of Modeling[6]:

- Empirical risk scores determined and patient outcomes compared
- Risk scores are relative to reference cases= dengue, 9-45 year old, 2008, no comorbidities
- Measure of risk of death: Log odds ratio

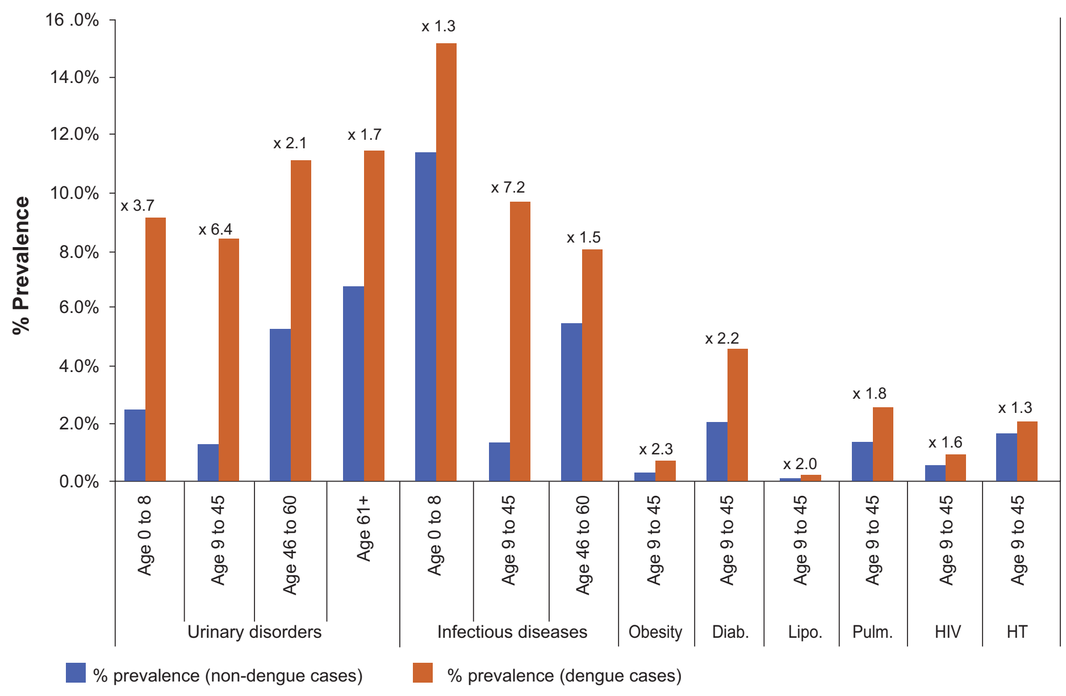
Tools

- Cox survival for Duration and Logistic regressions for Death and ICU admission after controlling by potential confounders (as age, year of inclusion).

RESULTS

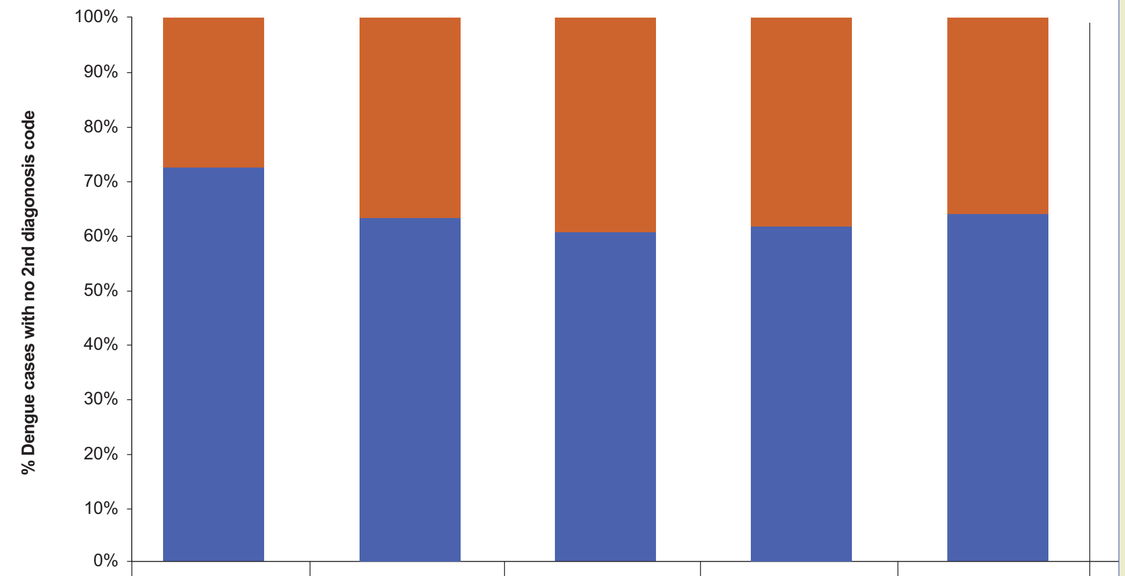
Prevalence of Risk factors

Comorbidities with increased prevalence in hospitalized dengue patients by age



- Increased urinary disorder, infectious diseases, obesity, diabetes, pulmonary disease, HIV, hypertension in 9-45 yo

Severe hospitalized dengue affects all ages but majority of cases occur in preadolescents and adults (9 + yo)

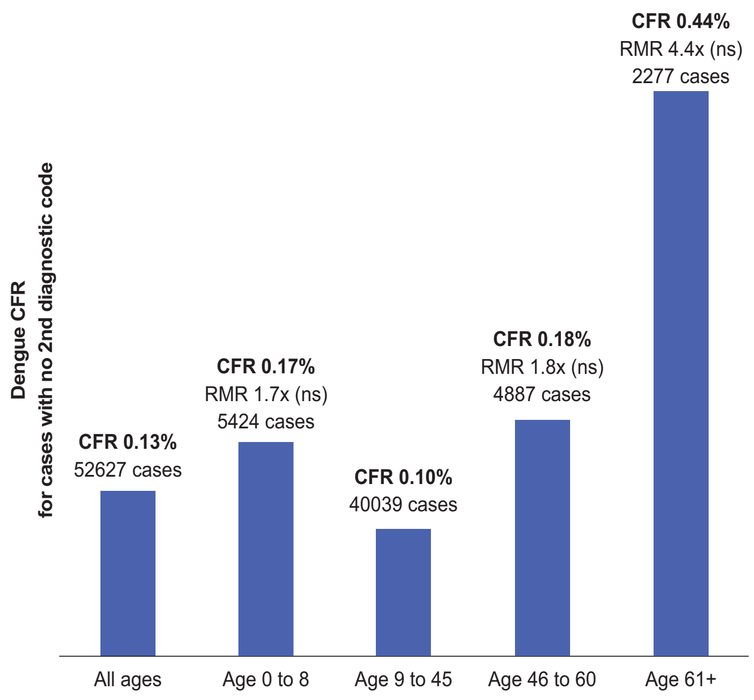


	Age 0 to 8	Age 9 to 45	Age 46 to 60	Age 61+	All ages
DHF (A91)	1463	14483	1921	862	18729
DF (A90)	3961	25556	2966	1415	33898

- Over 1/3 cases were severe dengue (DHF)

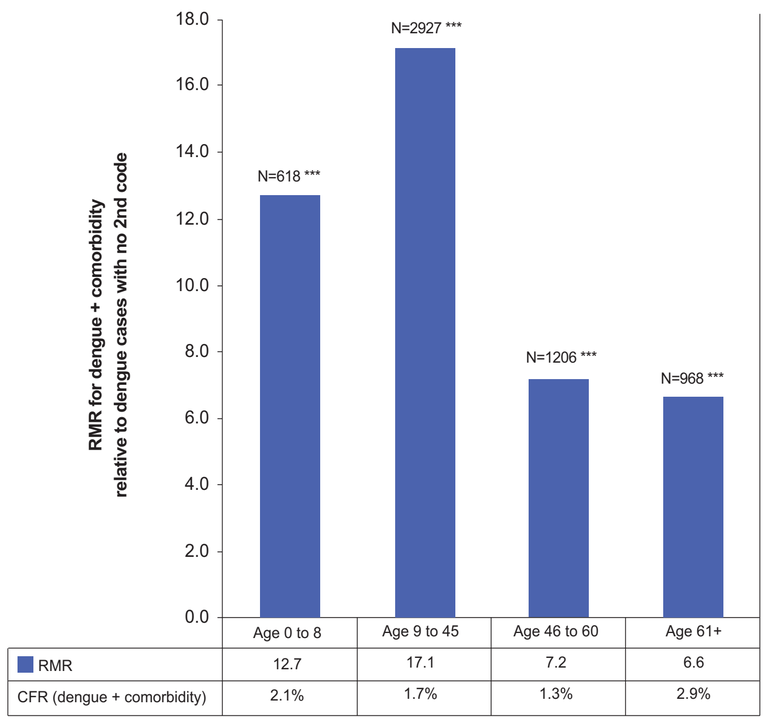
Mortality Rates

Risk of Death from hospitalized dengue is higher in children and older adults 61+



- RMR 4.4 (60+ yo) compared to younger patients (9-45 yo)

Risk of hospitalized dengue death is higher in the presence of common comorbidities at any age



- 17 times higher in 9-45 year-olds

Comorbidities increase hospitalized Dengue mortality at any age

Age (yo)	Comorbidity	CFR (%)	RMR	95% CI	P value
0-8	Renal disease/failure	4	26	3-199	<0.05
	Pulmonary disease	3	16	5-50	<0.001
	Infectious disease	2	15	6-39	<0.001
9-45	HIV	6	63	27-146	<0.001
	Pulmonary disease	5	54	30-98	<0.001
	Renal disease/failure	5	53	29-98	<0.001
	Obesity	3	27	7-111	<0.01
	Infectious disease	2	23	14-39	<0.001
	Diabetes	0.9	9	3-24	<0.01
46-60	Pulmonary disease	8	43	15-125	<0.001
	Renal disease/failure	4	19	5-70	<0.001
	Infectious disease	1	7	1-31	<0.05
	Diabetes	0.6	4	1-11	<0.05
61+	Ischaemic heart disease	11	24	6-102	<0.001
	Pulmonary disease	8	19	8-47	<0.001
	Renal disease/failure	7	16	6-42	<0.001
	Infectious disease	4	8	3-25	<0.01
	Diabetes	3	7	3-15	<0.001
	Hypertension	2	4	1-10	<0.05

CFR=Case fatality rate

RMR= Relative Mortality Ratio (comorbidities compared to dengue alone)

- Pulmonary disease, infectious diseases, renal disease/failure, diabetes (ischaemic heart disease 46+ yo)

CFR and hospital duration incrementally increased in dengue patients with more comorbidities

		DENGUE CASES			DURATION (DAYS)	
Diagnosis codes	Cases (%)	Cases	Deaths	CFR (%)	Mean	St. dev.
1 (Principal only)	77	52627	68	0.1	3.0	2.4
2	17	11362	77	0.7	3.4	2.6
3	5	3121	49	1.6	4.0	3.5
4	1	815	50	6.1	4.8	4.8
5	0.3	180	13	7.2	5.2	5
6	0.1	79	9	11.4	8.3	10
7	0	10	1	10	16.9	28.2
All dengue cases	100	68194	267	0.39	3.2	2.6

- CFR increased from 0.1 % to 10%, and hospital duration increased from 3 to 16.9 days with an increase in the number of secondary diagnosis in dengue patients.

Modeling

- Risk of death from severe dengue was ~2 fold higher than death from diabetes
- Duration of hospital stay, ICU admission and death are strongly correlated

Age, dengue severity, comorbidities are independent and cumulative risk factors for longer hospital duration, ICU admission and death

RISK SCORES[6]	Duration	ICU	Death
COMORBIDITIES			
Pulmonary disease	23	38	38
Ischaemic heart disease (IHD)	43	-195	51
Renal disease/failure	25	20	35
Diabetes	5	-1	8
Hypertension	-7	18	-7
Dyslipidaemia	-193	-201	-169
DENGUE SEVERITY			
Dengue	0	0	0
Severe dengue (DHF)	14	14	18
AGE			
0 to 8	6	1	7
9 to 45	0	0	0
46 to 60	6	-9	7
61+	16	-12	20

CONCLUSIONS

- **In Mexico, severe hospitalized dengue occurred at any age but the majority of cases were in pre-adolescents and adults.**
- **At any age, risk of dying from hospitalized dengue was even higher with common comorbidities such as pulmonary disease, renal disease, diabetes, ischaemic heart disease, obesity and HIV**
- **CFR and hospital duration incrementally increased in dengue patients with more comorbidities**
- **Comorbidities, younger and older age, severe dengue are independent and cumulative risk factors for longer hospital duration, increased intensive care admission and in-hospital death**
- **Ensuring access to dengue preventative measures in individuals 9 years and above including those with comorbidities could help these countries achieve the WHO objective of 50% reduction in mortality and 25% reduction in morbidity due to dengue by 2020**

References

1. The Global Economic Burden of dengue: a systematic analysis. DS Shepard Lancet Infect Dis 2016:935-41
2. Relevance of Non-communicable comorbidities for the development of the severe forms of dengue: A Systematic Literature Review. J. Toledo PLOS Negl Trop Dis 2016 4;10(1):e0004284.
3. Secretaría de Salud, México: Subsistema Automatizado de Egresos Hospitalarios (SAEH) 2008-2015: http://www.dgis.salud.gob.mx/contenidos/basesdedatos/std_egresoshospitalarios_gobmx.html
4. Big data analytics in healthcare: promise and potential. W. Raghupathi, V. Raghupathi. Health Inf Sci Syst. 2014; 2: 3
5. a) KEM® (Knowledge Extraction and Management) data mining platform, Ariana Pharmaceuticals S.A.; b) M Liquiere, J Sallantin, Structural Machine Learning With Galois Lattice and Graphs. ICML'98: 5th International Conference on Machine Learning. Madison, WI: 1998; 305-313
6. Biglm: bounded memory linear and generalized linear models. T Lumley 2013
7. KNIME, The {K}onstanz {I}nformation {M}iner. M. R. Berthold et al. Studies in Classification, Data Analysis, and Knowledge Organization. 2007

Disclosures

- This study was sponsored by Sanofi Pasteur including service provision of database consolidation, data mining and analysis by Ariana Pharmaceuticals