

Data Analysis on SARS Clinical Management

Hospital Authority
16 Aug 03



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HA SARS Collaborative Group

Purpose

- To steer, coordinate, enhance, report and disseminate latest information on SARS management

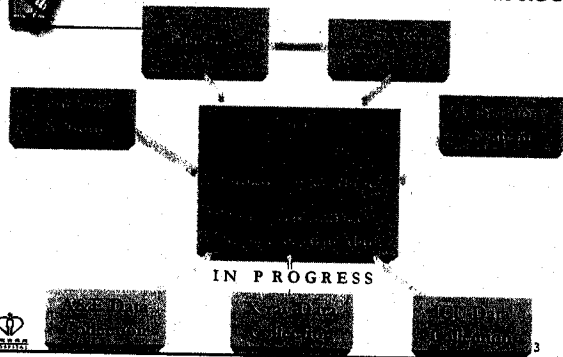
Membership

- Clinicians with contributions and expertise in SARS management
 - Physicians, paediatricians, geriatricians, intensivists, radiologists, microbiologists, pathologists, psychiatrists, rehabilitation and A&E specialists



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SARS Central Clinical Database



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Contents

Hong Kong Data

- Risk and prognostic factors
- Study on Kaletra treatment
- Study on steroid usage

International Comparison

- Treatment
- Outcome and Case Fatality Rate



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Risk and Prognostic Factors



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Risk/Prognostic Factors + Drug Treatment vs Outcome

Model on Aged 15-74 only (n=889)

Death vs Discharge	Discriminant Analysis	Logistic Model	
	Standardised Canonical Coefficient	Adjusted Odds Ratio	p-value
Age	0.51	1.98 (per 10 years ↑)	<0.0001*
LDH - 1 st reading	0.41	1.02 (per 10 IU/L ↑)	<0.0001*
Comorbidity	0.39	3.39 (vs without)	0.0002*
Lowest SaO ₂ before intubation	-0.29	0.92 (per 1% ↑)	<0.0001*
Neutrophil - 1 st reading	0.23	1.12 (per 10 ⁹ /L ↑)	0.01*
Sex	0.20	2.38 (vs F)	0.002*
Ever Steroid	0.07	1.02 (vs No Steroid)	0.98
Ever Ribavirin	0.06	1.15 (vs No Ribavirin)	0.85
	Overall model: p < 0.0001 Canonical correlation: 57.1 %	Overall model: p < 0.0001	



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Study on Kaletra Treatment



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Kaletra®

- Lopinavir/Ritonavir combination
- Lopinavir - Aspartate Protease Inhibitor used in HIV infection
- Protease found in Coronavirus
- Lopinavir found to have weak in vitro effect on Coronavirus



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Analysis of Kaletra Use

	Kaletra Subjects	Matched Cohorts*
n		634
Treatment	Ribavirin/ Steroid	Ribavirin/ Steroid

*Matched for age, sex, comorbidity & initial LDH level



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Discussion

- Early treatment with Kaletra and Ribavirin
 - Lower death rate
 - Lower intubation rate
 - Reduced use of pulsed corticosteroid
- Need for a randomised controlled study of Kaletra and Ribavirin vs Placebo



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Study On Steroid Usage



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Analysis on Treatment with Steroid

- Group 0 : Had not received corticosteroid
- Group I : Had received corticosteroid
- Group II : Had received corticosteroid and additional pulsed methylprednisolone (MP) for 1 course (0.5 - 3g MP within 6 days)



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Discussion

- Limitations of a retrospective study
- Compared to Group 0, Group I patients given steroid had no differences in outcome except longer time to discharge and time to death → RCT on steroid vs no steroid
- The more severe respiratory failure in Group II when treated with pulsed steroid produced similar outcome as Group I → RCT on pulsed steroid?



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International Comparison



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Treatment

Study	n	Anti-biotics	Antiviral (Ribavirin)	Steroid	Pulsed MP	Ventilation
Hong Kong	Chu A:44v634 B:31v343		2-4g once → 3.6g/d (+ Kaletra)	MP:150mg/d	1.5-5g	A:NI-0%;M-4% B:NI-3%;M-10%
	Lee 138	β lactam & macrolide or levofloxacin	1-2g/d (or 3.6g/d po)	P:50mg/d	1-1.5g	NI-0%;M-14%
	So 31		1-2g/d x3 → 2.4g/d po x14	MP:150mg/d	2g	NI-13%;M-0%
	Peiris 75		1-2g/d x14	HC:0.6g/d x10 → P:50mg/d	1.5g	NI-4%;M-14%
Canada	144	95%	88% 2g once → 4g/d x4 + 1.5g/d x3	40% HC 1-2.5g/d	Nil	NI-0%; M-14%
Singapore	192	~11K	7% 1g/d	4% of non-ICU patients	0.6g	NI-0%
Guangzhou	193	Macrolide + quinolone	1.4-1.6g/d	MP:80-160mg/d	0.24-0.48g	NI-25-40%

MP: Methylprednisolone, P: Prednisolone, HC: Hydrocortisone, NI: Non-Invasive, M: Mechanical

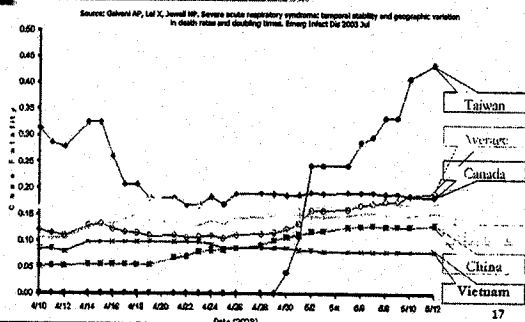
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Case Fatality Rate



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Cumulative Case Fatality Rates- 10 Apr to 12 May



International Comparison of CFRs in Relation to Case Mix

	No of Cases ¹	CFR ¹	Median Age ¹	Co-morbidities (%)	LDH ≥ 230 (%)	HCW (%) ¹
Canada	251	17	49 (1-98)	-	-	43
China	5327	7	-	13 ²	46.5 ³ 18 ² 26.3 ³	19
Hong Kong	1755	17	40 (0-100)	17.8 ⁴	67.8 ⁴	22 (HA staff: 19)
Singapore	238	14	35 (1-90)	-	-	41
Taiwan	665	27	46 (2-79)	-	-	13
USA	33	0	36 (0-83)	-	-	3
Vietnam	63	8	43 (20-76)	-	-	57



1. WHO (released on 15 Aug 03)
2. Xiao et al, 78 patients
3. Zhao et al, 190 patients

4. n = 1883
5. n = 1471

6. Zhang et al, 260 patients
7. n = 1671

Age-stratified Case Fatality Rate

Age Group	CFR	Cum. Age	CFR
<24	0%	0-24	0%
25-34	2%	0-34	1%
35-44	10%	0-44	4%
45-54	13%	0-54	6%
55-64	25%		
65-74	47%	0-74	12%
>75	66%	0-100	17%



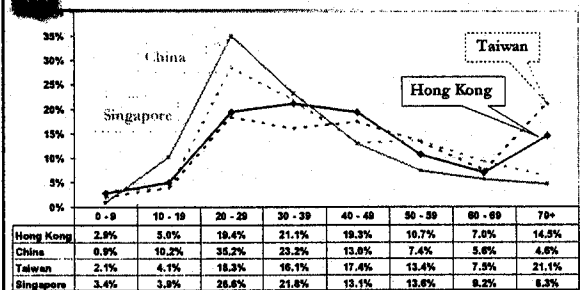
Case Fatality Rate Comparison

Age Group	Hong Kong	WHO
0-24	0%	<1%
25-44	6%	6%
45-64	16%	15%
65+	58%	>50%

In HK: 60% deaths >65 yrs,
40% deaths >75 yrs



Age Distribution of SARS Cases



If age profile similar to China → CFR 9.3 %



>65 & Comorbidity Among Fatalities

	≥65	<65
With Co-Morbidity	39%	11%
Without Co-Morbidity	19%	31%

* If 13% with comorbidity (instead of 17.8%) → CFR 14.5 %



Comorbidity Case Fatality Rate

- Chronic renal failure – 89%
- Cerebral vascular accident – 71%
- Ischaemic heart disease – 65%
- Chronic liver disease – 60%
- Diabetes mellitus – 50%
- Cancer – 49%
- Chronic obstructive airway disease / Asthma – 38%

* If 13% with comorbidity (instead of 17.8%) → CFR 14.5 %



Health Care Workers

HA HCWs

- 19% of total SARS patients
- CFR 2%
- Young
- Healthy
- 74% female

* If HCW 50% → CFR 6.1 %



International Comparison of Mortality Figures in ICU Subgroup

	Hong Kong	Toronto (JAMA, July 2003)	Singapore (JAMA, July 2003)
N (Total in cohort)	1755	196	199
Rate of ICU admission (%)	21.7	19	23
Rate of Intubation (%)	14.0 ¹	14.8	-
Mortality of ICU patients (%)			
- 28 days after symptom onset	22.3 ¹	-	37
- 28 days after ICU admission	26.7 ¹	34	-
- Overall	43.3 ²	-	-
Mortality of whole cohort at 28 days after symptom onset	10.7 ¹	-	10
Mortality of whole cohort	17	-	-

1. n = 1552 2. n = 337 out of 1852 patients with complete records 25

International Comparison of Mortality Figures in Relation to Intubation / NIV Status

	Hong Kong	China (GZ, Zhang et al)	China (GZ, Xiao et al)	China (GZ, Zhao et al)
N (Total in cohort)	1755	260	78	190
Rate of ICU admission (%)	21.7	-	34.6	-
Rate of Intubation (%)	14.0 ¹	4.2	19.2	6.8
Rate of NIV (%)	2.0 ¹ (BIPAP)	13.8	30.8 (CPAP)	32.6 (CPAP)
Mortality				
- 28 days after symptom onset	10.7 ¹	-	-	-
Overall	17	4.2	9	5.8

1. n = 1552 26

Over-reporting of non-CoV

CoV positive

Hong Kong - 60%

USA - 12% (8 out of 68)

* If PCR 12% POS in HK → CFR 9.6%

Source: WHO's Global Conference on SARS held in Malaysia on 17-18 June 03

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Discussion- Confounding Factors in Interpreting CFRs

Case mix

- CFR affected by case mix: age, comorbidities, HCW, LDH ...
- If age profile similar to China → CFR 9.3 %
- If comorbidity 13% → CFR 14.5 %
- If HCW 50% → CFR 6.1 %

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Discussion- Confounding Factors in Interpreting CFRs (cont'd)

Timing

- If 28-day fatality is used → CFR 10.7%

Inclusion Criteria

- If dilution of denominator by non-SARS or mild SARS to give CoV positivity of 12% → CFR 9.6 %

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Summary

- Risk & prognostic factors influence interpretation of treatment outcome
- Useful initial findings :
 - Early treatment with Kaletra and Ribavirin
 - Pulsed methylprednisolone for severe cases
- Need to prepare RCT protocols for next epidemic
- The CFR of Hong Kong compared favourably with overseas countries

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