Hospital Based Infectious Disease Related Proportional Mortality Study

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ABSTRACT

Objective: To understand the temporal trends in mortality in Rural Central India. **Design:** Retrospective review of physician issued death certificates from a rural teaching hospital. **Materials and Methods:** Physician issued death certificates from 1979 to 2008, available with a rural teaching hospital were analyzed and information on age, gender, date, and cause of death was abstracted. We estimated cause-specific, proportional mortality ratio (PMR) stratified by age, and gender. We compared the difference in PMR in first fifteen years of the study period (period A, 1979-1993) with the later (period B, 1994-2008). **Results:** We found 20494 death certificates between 1979 and 2008. Proportion of infectious disease related mortality declined from 35% in 1979-1983-26% in 2004-2008. In the same periods, injury related mortality increased from 4.6% to 13.4%, and chronic disease mortality from 19% to 28%. The absolute difference in PMR (per 1000 deaths) was statistically significant between period B and period A, for infections (a decline of 80.67 [95% CI 66.97-94.03]), chronic diseases (an increase of 45.85 [95% CI 33.49-58.55]), and injuries (an increase of 42.98 [95% CI 33.87-52.26]). **Conclusion:** Temporal trend in mortality from a single hospital in rural Central-India over the past three decades shows decline in infectious diseases, and rise in injuries and chronic diseases.

Key words: Mortality, Rural India, Temporal pattern

INTRODUCTION

Epidemiologic transition from infectious diseases to chronic diseases has been a hallmark of demographic change in the twentieth century.[1] This change has been contributed by a complex process of aging populations, success of infectious disease control programs, and economic development contributing to a life-style change. In the past two decades, such a transition has been reported from urban low-and-middle-income countries (LMICs).[2-4] More recently however, such a change has also been documented in the rural areas.[5-7] Globally chronic cardiovascular diseases are now the leading cause of death, with 6 of every 10 deaths due to this cause.[8] In a cross-sectional study from rural Andhra Pradesh in India, a third of all deaths were due to chronic diseases, followed by injuries and infectious diseases.[6]

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Mortality records in LMICs are deficient, and registration systems for cause of death are weak.[8] As a result most mortality studies rely in verbal autopsy methods, which depend on recall of events by the deceased family members. Most mortality studies from LMICs are based on verbal autopsy methods.[5,6,9-13] In some other studies, the duration of recall in verbal autopsy methods is longer than a decade.[5,10] It is estimated that the uncertainty in the cause of death is up to 15-20% in LMICs, largely due to differential data availability.[8] This uncertainty is likely to be more, when we study temporal patterns of mortality from the distant past. Another source of mortality information is physician issued cause of death certificates. Since these are prepared at the time of death, with all available clinical information, these are likely to be more accurate. However, in India only a small proportion of all deaths occur in the hospitals, excluding those who are economically disadvantaged, and those choosing not to seek advanced medical care. Thus, despite the cause of death being more accurate, generalizability of this data source to an entire population is likely to be poor. Given the trade-offs involved with both verbal autopsy and certified cause of death, both these methods complement each other.

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Evidence of epidemiological transition in India is largely based on cross-sectional studies performed in different settings and regions in the past.[14] Most mortality studies from India have sampled deaths from a short period of time,[6,15] and only one study has evaluated long-term trend, but based on verbal autopsy methods.[5] Thus, there exists a gap in our understanding of mortality trend, especially from rural India. We performed this study to understand the temporal trends in mortality (based on physician issued death certificates) across all age-groups from a hospital in the Rural Central India.

MATERIALS AND METHODS

Setting

The study was conducted in Kasturba Hospital Sevagram, which is a 648-bedded teaching hospital. The teaching hospital was setup in 1969 at Sevagram, as a rural teaching institute. Treating physicians certify all deaths that take place in the hospital, and issue a three-part death certificate as per WHO guidelines. All death certificates are filed with the medical records department of the hospital. We conducted a review of death certificates from the hospital. The institutional ethics committee approved the study design. No personal identifiers were collected from the death certificates.

Data collection

We conducted a survey of all deaths, which had taken place in the hospital from 1979 to 2008. We chose this study period as death certificates prior to this were not available. We physically examined each death certificate, and collected information about age and gender of the deceased, date month and year of death, and primary cause of death on the certificate. We used the above primary information to construct three secondary variables. First, two investigators classified each cause of death as per international classification of disease (ICD-10). We categorized each ICD-10 code into eight categories (Infections, chronic diseases, injuries, malignancies, maternal, perinatal/congenital, miscellaneous, and unclassified). This categorization is provided in [Table 1]. Second, we categorized time in six calendar-year intervals (1979-1983, 1984-1988, 1989-1993, 1994-1998, 1999-2003, 2004-2008). Each of these intervals is of 5-year duration. Third, we categorized age at death as less than 1 month (neonatal), 1 month to 1 year (infant), 1-12 years (child), 13-35 years (young adult), 36-60 years (middle aged), and 60 years or more (elderly).

Table 1: Classification of diagnoses into categories and sub-categories

Disease category	Code	Disease sub-category
Infectious diseases	1.1	Diarrhea
	1.2	Pneumonia
	1.3	Ac encephalitis syndrome
	1.4	HIV
	1.5	Septicemia
	1.6	Malaria
	1.7	Tuberculosis
	1.8	Tetanus
	1.9	Others
Malignancies	2.0	All malignancies
Chronic diseases	3.1	Acute coronary syndromes
	3.2	Cerebrovascular conditions
	3.3	Diabetes mellitus/hypertension
	3.4	Rheumatic heart disease
	3.5	Chronic hematologic diseases
	3.6	Chronic respiratory diseases
	3.7	Chronic kidney conditions
	3.8	Chronic hepatic conditions
	3.9	Others
Maternal mortality	4.0	All maternal deaths
Perinatal causes	5.0	All perinatal causes, and congenital anomalies
Injuries	6.1	Trauma or hemorrhage
	6.2	Burn
	6.3	Poisonings
	6.4	Venomous bites
	6.5	Other
Miscellaneous	7.1	Post-operative death
	7.2	Acute gastrointestinal cause
	7.3	Acute hepatic cause
	7.4	Acute renal and endocrine cause
	7.5	Anemia and nutritional
	7.6	Dermatologic
	7.7	Neurologic
	7.9	Others
Unclassified	8.0	All unclassified (cause mentioned either as cardiopulmonary arrest, or cause to be determined after a post-mortem)

HIV: Human immunodeficiency virus

Statistical analysis

We entered data in Epidata software, and analyzed using the statistical software STATA version 12 (College Station, TX). We performed a descriptive analysis and determined number of deaths in each disease, time-period, and age categories. We estimated proportional mortality ratio (PMR) by disease categories in each time and age categories. We compared the difference in PMR in first fifteen years of the study period (period A, 1979-1993) with the later (period B, 1994-2008) across disease and age categories. These study periods were so defined as PMR for infectious and chronic diseases showed a reversal in these time-periods. We used Chi-square test to evaluate if the difference in PMR in periods A and B was significant ($P < 0.01$ as a level of significance).

RESULTS

We found 20494 death certificates between 1979 and 2008 in hospital records and included these in the analysis. A total of 39.4% of these deaths were in females, and 17% in elderly. In each time period, number of hospital admissions as well as deaths showed an incremental rise. Overall deaths were 3.3% of hospital admissions, which significantly correlated with hospital admissions ($r = 0.94$, $P < 0.001$). PMR for infections showed a declining trend while that for chronic diseases and injuries showed a rise across time-periods [Table 2]. Proportion of infectious disease related mortality was 35.1% in 1979-1983, which declined to 26.1% in 2004-2008. In the same periods, injury related mortality increased from 4.6% to 13.4%, and chronic disease mortality from 19.2% to 28.7%. In the first two time-periods (1979-1983, and 1984-1988) proportion of mortality due to infectious causes was greater than chronic diseases and injuries put together. After 1994-1998, proportion of chronic disease mortality became higher than infections while mortality due to injure remained constant [Figure 1]. A total of 6617 deaths took place between 1979 and 1993, and 13876 between 1994 and 2008. The difference in PMR (per 1000 deaths) was statistically significant across these time-periods for infections (a decline of 80.67 [95% CI 66.97-94.03]), chronic diseases (an increase of 45.85 [95% CI 33.49-58.55]), and injuries (an increase of 42.98 [95% CI 33.87-52.26]) [Table 3].

Reduction in proportional mortality due to infectious was consistent across age and gender categories [Table 4, Figure 2]. Reduction was significant in neonates, infants, children, and young adults, and overall reduction was similar in females and males. We compared PMR across disease subcategories. We found that reduced mortality due to diarrhea, encephalitis, septicemia, tuberculosis, and tetanus contributed to decline in PMR for infectious etiologies. PMR for pneumonia remained unchanged while that for malaria and human immunodeficiency virus increased across periods A and B [Figure 2].

Rise in proportional mortality due to injures was significant in children, young adults, and middle-aged [Tables 3 and 4]. There were some important gender differences in mortality pattern as the increase in PMR due to injuries was significantly more in females as compared to males (67.65 vs. 26.71 per 1000 deaths, $P < 0.0001$) [Figure 2]. This difference was largely because of more deaths in females due to burns in the 13-35 year and 36-60 year age-groups. Of the 1553 deaths due to burns, 1236 (79%) were in females. Of the 481 deaths due to poisoning, 155 (32%) were in females. Burns and poisonings significantly contributed to a rise in proportional mortality due to injuries.

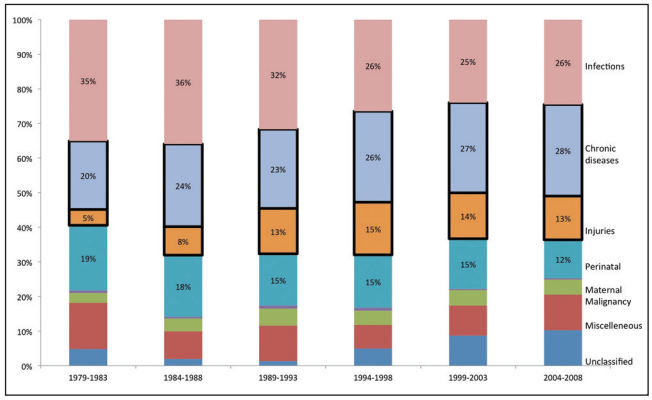

Figure 1: Bar chart showing proportional mortality ratio of each disease category in five year time periods ($n = 20494$)

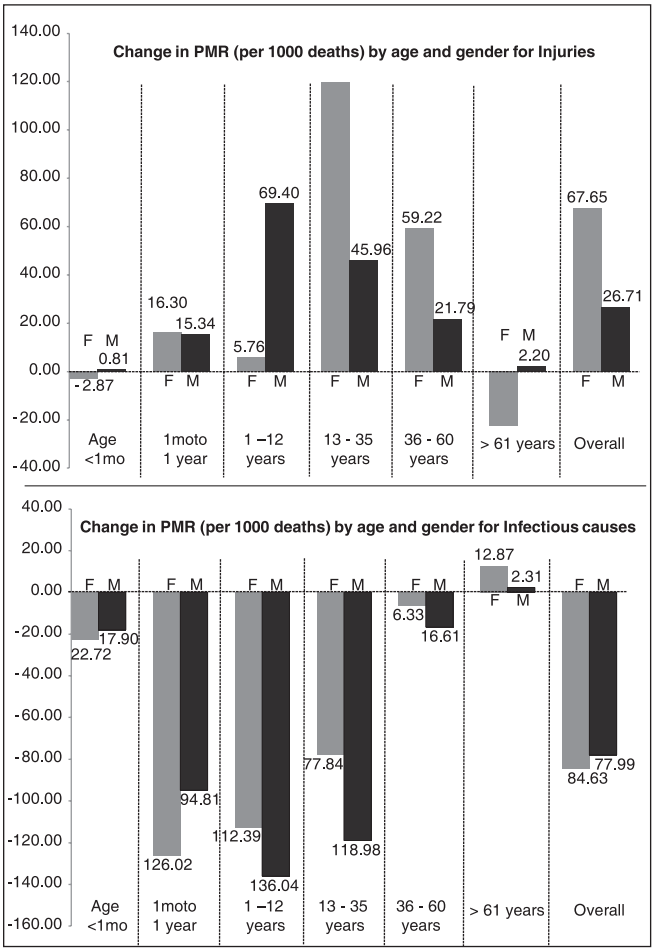

Figure 2: Gender differences in proportional mortality ratio for injuries and infectious causes. The numbers represent change in proportional mortality ratio in period 1994-2008 as compared to 1976-1993. Negative values indicate a decline in mortality, and positive values indicate a rise. Grey bars are for females (F) and black bars are for males (M). The gender differences have been stratified by age categories

Table 2: Frequency and proportional mortality ratio of cause of death in each disease category in each time-period (*n* = 20494)

Variable	1979-1983	1984-1988	1989-1993	1994-1998	1999-2003	2004-2008
Hospital admissions	60864	67529	78040	94685	132229	173636
Number of deaths	1200	2457	2961	3669	4870	5337
Percent deaths	1.97	3.64	3.79	3.87	3.68	3.07
Disease category*						
Infectious diseases	421 (35.1)	882 (35.9)	937 (31.6)	972 (26.4)	1212 (24.8)	1396 (26.1)
Chronic diseases	237 (19.7)	588 (23.9)	679 (22.9)	964 (26.2)	1318 (27.0)	1504 (28.2)
Injuries	55 (4.6)	202 (8.2)	388 (13.1)	558 (15.2)	672 (13.8)	719 (13.4)
Malignancy	34 (2.8)	90 (3.6)	146 (4.9)	150 (4.1)	227 (4.6)	250 (4.7)
Maternal	9 (0.7)	12 (0.5)	25 (0.8)	31 (0.8)	17 (0.3)	21 (0.4)
Perinatal/congenital	226 (18.8)	438 (17.8)	443 (14.9)	561 (15.3)	732 (15.0)	630 (11.8)
Miscellaneous	160 (13.3)	198 (8.1)	304 (10.2)	250 (6.8)	253 (5.2)	233 (4.3)
Unclassified	58 (4.8)	47 (1.9)	39 (1.3)	183 (4.9)	439 (9.0)	584 (10.9)
Brought dead	0 (0)	2 (0.08)	2 (0.07)	64 (1.74)	68 (1.40)	11 (0.21)
Cardiac arrest	57 (4.75)	43 (1.75)	34 (1.15)	16 (0.44)	25 (0.51)	46 (0.86)
MLC death<24 h	1 (0.08)	2 (0.08)	3 (0.10)	103 (2.81)	346 (7.10)	527 (9.87)

*All values for disease categories indicate number (PMR in percent) for the specified time period. MLC: Medico-legal case, where death occurs in less than 24 h of hospitalization, and attending doctor writes cause of death "to be decided after post-mortem". PMR: Proportional mortality ratio

Increased mortality due to cerebrovascular diseases and chronic liver disease contributed to a rise in PMR for chronic diseases. PMR for other chronic diseases remains unchanged. There was no consistent rise in chronic disease PMR across age categories. Age-stratified PMR due to perinatal or congenital causes was not different in neonates, and significantly higher in infants. There was no significant difference in maternal mortality, and mortality due to malignancies [Tables 3 and 4].

Deaths categorized as unclassified were from three broad categories. First, those patients who were dead on arrival (brought dead) and proportion of such deaths significantly increased in period B. Second, those where a foul play was suspected, law enforcing authorities were informed, and death occurred within 24 h of hospital admission (medico-legal death < 24 h). In such cases, treating doctors usually write "cause to be decided after post-mortem." Third, where the primary cause of death is missing, and cause of death is written as cardiac or cardio-respiratory arrest. Proportion of deaths in this category was small and reduced in period B [Tables 2 and 3].

DISCUSSION

In the current study of causes of in-hospital mortality over three decades, we found a significant and consistent reduction in deaths due to infectious etiologies, and rise in deaths due to injuries and chronic diseases. Proportion of mortality due to other etiologies remained unchanged. These findings suggest epidemiological transition in causes of mortality, as after 1998 infectious diseases were no longer the single largest contributor to mortality. These findings from Rural Central India document important gains in infectious disease control, and suggest injuries and chronic diseases as future disease control priorities.

These results need to be interpreted carefully as these represent a small proportion of all deaths in the community, which occurred at a single hospital. While the population of Wardha district increased by 57% from 0.82 million (1981) to 1.29 million (2011), number of hospital admissions as well as deaths increased by more than three-folds. This suggests increased health seeking and possible increase in the catchment population of the hospital beyond a single district. However, these factors are likely to have a minimal impact on PMR, as the proportion of deaths to hospital admissions remained similar across time-periods. Other factors such as increasing longevity and more births change demographic structure of the population. Standardized mortality rates are used to adjust for these effects at a population level, we however, limited ourselves to proportional mortality rates, as our study was limited to a single hospital. While our study is deficient in this regard, it is informative about the trend in mortality over a long period.

While studies from the developed countries, where death-records are available for longer than hundred years showed a decline in infectious diseases and rise in chronic diseases around 1950s,[16] such a change has been more recent in LMICs. Most compelling evidence about epidemiological transition comes from a study from rural Bangladesh.[7] This study used concurrent verbal autopsy methodology with recall period of less than 4 weeks from 1986 to 2003,

Table 3: Difference in proportional mortality across two time periods (1979-1993 versus 1994-2008) by disease categories

Disease category	Period A (1979-1993)		Period B (1994-2008)		Difference in PMR	
	Number	PMR (per 1000 deaths)	Number	PMR (per 1000 deaths)	Period B-Period A	*P* value
Total deaths	6617		13876			
Infectious diseases	2241	338.67	3580	258.00	−80.67	<0.0001
Diarrhea	79	11.94	57	4.11	−7.83	<0.0001
Pneumonia	317	47.91	687	49.51	1.60	0.27
Encephalitis	569	85.99	781	56.28	−29.71	<0.0001
HIV	0	0.00	61	4.40	4.40	<0.0001
Septicemia	627	94.76	971	69.98	−24.78	<0.0001
Malaria	10	1.51	243	17.51	16.00	<0.0001
Tuberculosis	417	63.02	598	43.10	−19.92	<0.0001
Tetanus	122	18.44	62	4.47	−13.97	<0.0001
Others	100	15.11	120	8.65	−6.46	<0.0001
Chronic diseases	1503	227.14	3788	272.99	45.85	<0.0001
Coronary artery disease	372	56.22	893	64.36	8.14	0.02
Cerebrovascular disease	465	70.27	1499	108.03	37.75	<0.0001
Diabetes/hypertension	89	13.45	228	16.43	2.98	0.10
Rheumatic heart disease	46	6.95	116	8.36	1.41	0.28
Sickle cell disease	27	4.08	71	5.12	1.04	0.31
Chronic airway disease	140	21.16	258	18.59	−2.56	0.21
Chronic kidney disease	130	19.65	214	15.42	−4.22	0.02
Chronic liver disease	120	18.14	364	26.23	8.10	0.0004
Others	114	17.23	145	10.45	−6.78	<0.0001
Injuries	645	97.48	1949	140.46	42.98	<0.0001
Trauma	151	22.82	241	17.37	−5.45	0.007
Burns	362	54.71	1192	85.90	31.20	<0.0001
Poisoning	84	12.69	398	28.68	15.99	<0.0001
Venomous bite	39	5.89	105	7.57	1.67	0.18
Other	9	1.36	13	0.94	−0.42	0.38
Malignancies	270	40.80	627	45.19	4.38	0.15
Maternal mortality	46	6.95	69	4.97	−1.98	0.07
Perinatal/congenital	1106	167.15	1923	138.58	−28.56	<0.0001
Miscellaneous	662	100.05	735	52.97	−47.08	<0.0001
Unclassified	144	21.76	1205	86.84	65.08	<0.0001
Brought dead	4	0.60	143	10.30	9.70	<0.0001
Cardiac arrest	134	20.25	87	6.26	−13.98	<0.0001
MLC death<24 h	6	0.90	975	70.26	69.35	<0.0001

PMR: Proportional mortality ratio, HIV: Human immunodeficiency virus. Negative values for PMR indicate reduction, and positive values indicate increase

and less than 12 weeks from 2003 to 2006. Of over 18000 deaths analyzed, chronic diseases comprised of only 8% of all deaths in 1986, but 52% of deaths in 2006. There was a significant decline in mortality due to communicable diseases.[7] In another study from rural Bangladesh, about two-thirds of all deaths in adults in 2003-04 was due to chronic diseases.[12] Rise in prevalence of chronic diseases has also been documented from rural India. In a mortality-study from Northern India,[5] which sampled deaths between 1992 and 2009 and used verbal autopsy methods to determine the cause of death, chronic non-communicable conditions were the leading causes of death (47.6%) followed by communicable diseases including maternal, perinatal and nutritional conditions (34.0%), and injuries (11.4%). Deaths due to cardiovascular diseases showed a significant rise, whereas deaths due to diarrheal diseases showed a decline.[5] In another mortality study from Southern India, which sampled deaths from 2003 to 2004,[6] chronic diseases of the circulatory system were the leading causes of mortality (32%), followed by injuries (13%) and infectious and parasitic diseases (12%). Results of our study are broadly consistent with these findings.

However, there are important differences. While there has been a consistent decline in mortality due to infectious diseases, and rise in mortality due to injuries the proportion of chronic disease mortality is inconsistent across age-strata. Although overall chronic disease mortality showed a rise, there was no significant change in chronic disease mortality within age-strata, especially in middle-aged and

Table 4: Difference in proportional mortality ratio stratified by age and disease categories (*n* = 20494)

Mortality	All	Disease category							
		Infection	Chronic diseases	Injuries	Malignancy	Maternal	Perinatal/ congenital	Miscellaneous	Unclassified
Age less than 1 month (neonates)									
Deaths in period A (1979-1993)	1150	69	0	2	0	0	1064	5	10
Deaths in period B (1994-2008)	1990	79	0	2	0	0	1849	5	55
Difference in PMR (per 1000), B-A		−20.30*		-0.73			3.93	−1.84	18.94*
Age 1 month to 1 year (infants)									
Deaths in period A (1979-1993)	417	327	3	4	2	0	31	42	8
Deaths in period B (1994-2008)	433	293	10	11	1	0	62	29	27
Difference in PMR (per 1000), B-A		−107.50*	15.90	15.81	−2.49		68.85*	−33.74	43.17*
Age 1-12 years (children)									
Deaths in period A (1979-1993)	789	532	50	48	14	0	11	122	12
Deaths in period B (1994-2008)	733	404	63	74	20	0	11	92	69
Difference in PMR (per 1000), B-A		−123.11*	22.58	40.12*	9.54		1.07	−29.11	78.92*
Age 13-35 years (young adults)									
Deaths in period A (1979-1993)	1638	591	280	429	53	42	1	194	48
Deaths in period B (1994-2008)	3840	1016	543	1325	119	60	1	249	527
Difference in PMR (per 1000), B-A		−96.22*	−29.53	83.15*	−1.37	−10.02	−0.35	−53.59*	107.94*
Age 36-60 years (middle-aged)									
Deaths in period A (1979-1993)	1834	544	724	132	156	4	0	221	53
Deaths in period B (1994-2008)	4071	1150	1528	437	326	7	0	260	363
Difference in PMR (per 1000), B-A		−14.13	−19.43	35.37*	−4.98	−0.46		−56.64*	60.27*
Age 61 years or more (elderly)									
Deaths in period A (1979-1993)	790	178	446	30	45	0	0	78	13
Deaths in period B (1994-2008)	2809	638	1642	100	161	2	0	101	165
Difference in PMR (per 1000), B-A		1.81	19.99	−2.37	0.35	0.71		−62.78*	42.28*

PMR: Proportional mortality ratio. Negative values for PMR indicate reduction, and positive values indicate increase. *P values < 0.01

elderly. Further, it is expected for South Asia that 45% of all deaths will occur in age-groups of 60 years or more, 30% in 15-59 years, and 25% in those 14 years or less.[8] In our study only 17% of all deaths were in those above 60 years of age. This gap is likely to be due to reduced access to health-care among elderly, and it is likely that most of them would die at home. Thus, proportion of chronic disease mortality in our study is an underestimate. Cerebrovascular diseases were the most important etiology responsible for the rise in chronic diseases, consistent with other studies from rural areas.

Among infectious diseases, proportional mortality due to pneumonia remained unchanged while that of malaria increased. Mortality due to all other causes showed a decline. Thus, there are un-met challenges in infectious disease control. About a quarter of all deaths are still due to infectious diseases, representing a significant mortality burden. Another dramatic rise has been in injuries, especially burns and poisonings. About four-fifths of all burn, related mortality was among females. Most burn related deaths among women are either homicides or suicides, representing gender-inequality and social oppression. Most deaths categorized as "unclassified" are also likely to be due to injuries. While the rise in injury related mortality may partly be due to improved health seeking behavior especially among women, other societal and environmental factors are also likely. These include increased motor vehicles, reduced land-holdings, financial pressures, and higher stress levels. Many of these factors are however, speculative and further studies are needed to better delineate factors contributing to their rise.

Our study has certain strengths. Our study included only the physician certified in-hospital deaths, where determination of cause of death is likely to be more reliable. We included all available death certificates to minimize sampling bias, and two investigators classified all deaths to minimize information bias. However, our study has important limitations. First, we did not include deaths, which occurred outside the hospital. It is known that about one-third of all deaths take place either at home, or during transportation, especially in economically disadvantaged communities. In-hospital mortality may not be truly representative of overall mortality in the community. The deaths in elderly and in women are likely to be under-represented. Second, about 6% of all deaths were unclassified as in these cases either the primary cause of death was not mentioned, or cause was to be determined after post-mortem. Most of these are medico-legal deaths, especially after an injury,

either brought-dead to the emergency services or die after a brief stay in the hospital. Thus, the proportion of deaths due to injuries in our study is likely to be an underestimate, due to non-inclusion of unclassified cases. Third, this is a single-hospital study which has a predominantly rural catchment. Thus, while the results do-not represent urban areas, our results are likely to be similar with those in other similar settings. Fourth, while death certificates are likely to be more accurate than verbal-autopsy methods, their validity depends on training, experience, and information available with treating doctors. Over the three decades of the study period, more than hundred different doctors made decisions about the cause of death. Considerable inter-observer variability is expected in individual methods and information sources, in any study of this nature.

To conclude, temporal trend in mortality in rural areas over the past three decades shows decline in infectious diseases, and rise in injuries and chronic diseases. This trend documents epidemiologic transition, but also highlights the double burden of diseases which exists in rural India. We need effective strategies to address this double burden through public heath actions, which still have an infectious disease focus.

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